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# PATHOLOGY

FOR

# STUDENTS AND PRACTITIONER'S

An exhaustive bibliography is included in the third volume, (pages 2225 to 2452), with references to the literature of Germany, France, Spain, Italy, Sweden, Switzerland, Denmark, Portugal, Russia, England and the United States.

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For greater convenience a complete index is included in each volume and the volume number is printed in italics. The references to illustrations are in bold face type.

While there is in the text a complete system of cross references to related subjects the index summarizes them for ready reference. Example, under the heading "Abscesses" there are 76 entries.

# PATHOLOGY

## FOR STUDENTS AND PRACTITIONER'S

Authorized Translation of the
Lehrbuch der Pathologischen Anatomie

BY

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IN THREE VOLUMES 1072 ILLUSTRATIONS

VOLUME I

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# TRANSLATOR'S PREFACE

Kaufmann's Lehrbuch has seldom been far from the reach of the translator from the time he first began his work as a professional pathologist, and sections of it had already been translated for general use in this laboratory before the seventh and eighth editions appeared, therefore it was only natural that he should undertake the translation of the entire work into English. The task has been considerable, but the reward has been commensurate, not alone in clarifying and systematizing the knowledge gained in the translator's active pathological practice, but also in the pleasure of entering closely with the author into discussions of his favorite subject.

As a result of twelve years teaching experience; of intimate contact with many young and active hospital interns, also of close association with clinicians and patients who have presented their problems for solution, the translator has acquired a firm idea of how pathology should be taught to students of medicine so as to make them fit, when physicians, to take proper care of the sick. He believes that the most important thing a teacher of pathology can do is to help prepare students to become good doctors. Hence in the few paragraphs which the translator has felt called upon to add to the work, he has endeavored to emphasize the relationship of pathology to the sick and how the knowledge of that relationship can help the physician.

The translator has the fullest sympathy with the viewpoint that has been stressed so much in recent years, namely, that of pathological physiology, consequently the reader will find much upon this subject in the text. It is well to remember, however, before we can say, or even speculate on how a condition occurs, and what its dynamics are, that it is necessary to know what it is, and this we shall learn from Kaufmann's pathological anatomy. Of what avail is a discussion of the pathological physiology of atrophic cirrhosis of the liver, when, in reality, the liver about which we are speaking shows, not atrophic cirrhosis, but biliary cirrhosis, due to ascending cholangitis which is secondary to cholelithiasis?

Pathological anatomy is an art as well as a science, in fact, about 80% art and 20% science. It takes time and experience to acquire the necessary familiarity and knowledge to assign or designate lesions properly. This, the time devoted to pathological anatomy pure and simple, cannot, in fact, dare not, be slighted if pathological physiology and subsequent clinical medicine are to be mastered.

Then, there is the problem of tumor diagnosis: If it is important to have clinical insight into other pathological subjects, it is doubly important in this. It is not to confuse the medical student in his undergraduate studies, nor to deny the broad general principles of tumor diagnosis which have been taught to him, but merely to emplant a fact which should be implanted early, namely, that a correct diagnosis of many tumors cannot be made unless complete clinical data are submitted and considered in connection with the gross and microscopic pictures. And even then, we cannot always determine what the tumor is, but have to wait until time has elapsed and we have observed the sequelae in the patient. In other words, histological malignancy is not always biological malignancy, although, usually, it is; a section alone is not always sufficient to tell the whole story.

Naturally, many of those pathological conditions with which the translator has become especially familiar, such as diseases of the abdominal and thoracic viscera, could have been discussed in greater detail in the translation and his own point of view, or the point of view developed by the staff of The Lankenau Hospital as a group, could have been more emphasized. In most instances, however, it will be found that the author has at least mentioned them, so that, while the translator probably could have enlarged upon certain features, or thoughts, he feels that enough (little though it be) has been given to arouse the interest of the diligent reader.

The literature given by Kaufmann will be found in full, as in the German text. Some few references added by the translator will be found appropriately placed in the text itself.

Some liberties have been taken with subheadings and divisions, but in the main the original has been faithfully followed.

The drawings (considerably over one hundred) for the additional or supplementary pictures, which the translator thought would be materially helpful to the reader, were made by our staff artist, Mrs. W. B. Keighton (Eleanor M. Paxson) to whom he is deeply indebted for them. They are some of many which have accumulated in this laboratory during the last few years. These pictures are indicated by L. H. at the end of the legends.

The translator also has had much help, particularly from his assistant, Dr. C. E. Becker, and from Miss L. Snellbaker. He wishes also to record his thanks to Miss M. T. Shutt for her faithful writing of the manuscript, much from dictation, more by way of mechanical devices.

He also expresses thanks to the publishers for their patience and care throughout the preparation of this edition.

# PREFACE TO THE SEVENTH AND EIGHTH GERMAN EDITION

The sixth edition of this book was so well received at home and abroad in spite of its unusual size, that two reprints were necessary. In his endeavor to improve the subject matter of this combined edition, the author has increased the length and scope of each chapter so as to present as nearly as he could, a complete picture of our present objective knowledge. Thus the text has been enriched in many directions, particularly from experiences acquired during the World War.

An esteemed friend, a specialist in this line, was kind enough to say that the author had produced not merely a good text book with the didactic advantage of uniform conception and presentation, but a book suitable for reference by any one who required for whatever reason, a concise text book of special pathological anatomy; others were good enough to concur in this opinion. Students of medicine are always foremost in the author's mind, and thus the subjects which he regards as the most important for those who are to be our physicians, have been handled with special insistence and with detail; to complete the viewpoint, make it clearer to the understanding and at the same time to maintain interest, excursions are made into embryology, anatomy, physiology and general pathology.

Faithful to the thought that was expressed in the first edition of this work, the close connection between pathological anatomy and practical medicine, or between theory and practice, is emphasized by numerous references to clinical data. Readers who desire more details in any subject or who wish to trace all the sources, will, I hope, find the road well mapped out by the details in the text and by the references to the literature.

The number of illustrations is increased by several hundred, most of them from sketches made by the author of specimens in the Pathological Institute of Basle and in the collection at Gottingen. A number were also obtained from plates published in Virchow's Archives. Volume 3 contains the index and references to the literature which have been increased by many thousands. Although the latter occupies considerable space, this wealth of literature is indispensable in the opinion of his colleagues, Prof. Pio Foa and Prof. Sapegno, editors of the Italian translation of the book; the author, therefore, has not shirked the labor of its further extension; to ensure the utmost reliability he has included only such works as he himself has checked.

The author expresses his thanks to many colleagues in pathology and to numerous clinicians and specialists in other lines both at home and abroad for their kindness in sending him monographs and reprints; he hopes that this help will be forthcoming in the future also.

To Drs. Staemmler and Husten, the author also tenders his thanks for their valuable help in the preparation of the book.

EDWARD KAUFMANN.

GOTTINGEN

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# PATHOLOGY

## CHAPTER I

## ORGANS OF CIRCULATION

### HEART

#### PERICARDIUM

The pericardium is a serous membrane resembling a completely closed sac into which the heart has been pushed. Its wall consists of connective tissue rich in elastic fibres lined by an elastic basement membrane on which rests a single layer of low cells called endothelium or epithelium which become cubical to cylindrical during irritative processes and during regeneration, (see p. 8). The pericardio-pleuro-peritoneal cavity is formed from splitting in the mesoderm; its covering cells are modified mesenchyme or connective tissue cells, originally epithelial-like, almost cuboidal, but changing to flat serous endothelial cells. After death they quickly become detached; cilia have been demonstrated in these cells, (see Paladino, Kolossow, Muscatello, v. Brunn, lit.). The pericardium consists of two layers:

(*a*) The visceral layer or epicardium covers the heart and the proximal part of the large vessels—aorta and pulmonary arteries—to which structures it is firmly attached.

(*b*) The parietal pericardium surrounds the epicardium and the heart; it is quite distensible and elastic.

Malformations. Defects of the diverticuli and parietal layer, especially the left, are extremely rare; (Rohn, lit., Verse, Perna, Ebstein, Plaut, lit., Cameron, Lang).

A defect of the pericardium may accompany a sternal fissure, *i.e.*, a space in the sternum closed by fibrous tissue through which heart movements can be felt and seen during life. In ectopia cordis pectoralis (see malformations of the heart), the perfectly developed heart has no pericardium (Ect. nuda cordis) or may be surrounded by it.

##### Changes in Its Contents

The pericardium contains normally 5 cc. to 20 cc. of a clear yellow serous fluid, and more after a long agonal period.

If the fluid is absent at autopsy it is a post mortem phenomenon, because of evaporation towards the lungs, and the parietal layer may appear dry and like parchment on those areas where it is attached to a lung containing much air (emphysematous).

The pericardium has an almost reflecting sheen on account of its homogeneous cellular surface, its tendinous smooth structure, and the moistening with the serous fluid of the cavity. An increase of this normal fluid up to 150 cc. and more (1 litre and more) is called:

### Hydropericardium. Hydrops Pericardii

The fluid is amber colored or greenish, clear, contains albumen, is alkaline and called a transudate (non-inflammatory). But it frequently contains traces of fibrin which, on exposure to air, separate out as a cloudy gelatinous substance. Considerable amounts of fibrin are always a sign of an inflammatory exudate. Isolated round and endothelial cells, swollen and undergoing fatty degeneration, are almost always found in this hydropic fluid. The pericardial angles are rounded with the accumulation of the hydrops.

In the cadaver, the fluid often is stained red by absorption of blood coloring matters. When effusion of blood takes place during life and is followed by hemolysis, the fluid is stained a dirty brown or wine red color. In icterus, it is golden or bile yellow. With the cadaver in the dorsal position, the heart floats approximately in its normal position on the surface of the liquid (Schaposchnikoff, see against it, Damsch, and for it, Romberg).

**Etiology.**—Hydrops pericardii may be a concomitant of general anasarca whether from circulatory changes, stasis, or functional disturbances of the heart itself—cardiac hydrops—which may be chronic—heart lesions—or may only be agonal; or may be due to increased permeability of the vessel walls, blood changes—hydremia—or to cachexias from various causes, and especially chronic nephritis with disturbed renal function; hydrops may be idiopathic which is quite rare, and occasionally found in old people with cardiac atrophy (hydrops ex vacuo).

The transudate results from the passage of fluid blood constituents from the capillaries into the surrounding tissues, in this case to the surface of the serosa; according to Ludwig's theory, filtration, because of increased pressure within the vessels is the physical reason—or according to Cohnstein's theory, diffusion, a movement of fluid outward from the capillaries caused by osmotic pressure differences in which permeability operates in a way similar to that of a colloid; under pathological conditions, the fluid varies and thus there is a corresponding change in permeability

(Klemensiewicz). The physiological transudate is the lymph or blood lymph. Heidenhein's theory assumes it is formed by secretion of the endothelium of the capillaries. Hamburger applied this theory to the formation of hydrops. Thus in "mechanical hydrops" due to stasis, the secretory activity of the endothelium is influenced by blood stasis in such a way that the accumulation of metabolic products stimulates the endothelium to increased lymph secretion. Hydrops resulting from increased permeability of vessel walls is to be explained by assuming that the vessel wall loses the secretory function of the endothelium and becomes permeable like a filter, while in other cases it results from pathological stimulation of the capillary endothelium by lymph stimulants from pathological processes, especially of infectious origin; the action might be conceived as analogous to those demonstrated after administration of hirudin, decoction of crab muscle, peptone, and certain bacterial cultures. According to Asher's cellular physiological theory, secretion from tissue cells and the endothelium of lymph vessels and serous cavities is made responsible for the formation of lymph, *i.e.*, cavity hydrops, but without exclusion of transudation from blood vessels.

Absorption of a larger transudate is by reabsorption into blood vessels by diffusion. Absorption by lymph vessels must occur very slowly if at all under these conditions (Klemensiewicz).

**Consequences.**—In marked hydrops, there is demonstrable thinning of the parietal pericardium with disappearance of the epicardial fat, while the heart itself becomes smaller. Even in large accumulations in the pericardium, the work of the heart is remarkably little impeded, but the left lung may be displaced and compressed and thus interfere with cardiac activity.

> **Translator's Remarks.**—The pulsus paradoxus occurs during respiration, *i.e.*, a waxing and waning rhythmic pulse. The flow of blood into the heart is impeded by the increased intrapericardial pressure; pressure on the veins outside of the heart is increased and decreased during breathing; the difference thus varies in the pressures in the heart and in the veins, it being less during inspiration so that less blood can enter the heart. See *Katz L. N. & Gauchat H. W.;* Arch. Int. Med., 1924, 33, 371.

### Hemopericardium

The pericardium may contain blood. The membrane may be (*a*) intact, if, for instance, the heart ruptures and there is pure hemorrhage—or (*b*) there may be a disease accompanied by exudation, either simple or specific, usually tuberculous or carcinomatous, and the hemorrhage results

from newly formed vessels (compare hemorrhagic inflammation) and there is a mixture of blood and exudate. But there may also be a special tendency to hemorrhage on the basis of a dyscrasia, such as in scurvy, tuberculosis, carcinoma, etc.

If the pericardium contains large quantities, 200 cc. to 300 cc., rarely 500, even 800 cc., or up to several litres, after opening the thorax, it appears bulging, rounded, dark blue violet, or gray black, translucent, and displaces the lower parts of the lungs. Such conditions are seen: 1. under circumstances mentioned above (*b*); thus, occasionally, in tuberculous pericarditis, large quantities of almost pure blood are found. As a rule, striking functional disturbances of the heart are absent in these chronically developed blood mixed exudates. 2. An acute, pure hemorrhage into a healthy pericardium may occur in (*a*) spontaneous rupture of the heart wall, from chronic cardiac aneurysm, necrosis after occlusion of the coronary artery; high degree of fat infiltration, especially if combined with brown atrophy, usually in the left heart of old people; rarely with abscess, observed even in a suckling (Schaps); in acute parietal aneurysm (Hart), and finally in neoplasms and animal parasites (lit. by Romeick); (*b*) from rupture of aneurysms especially of the dissecting type, of the part of the aorta situated in the pericardium [for lit. and discussion of case in boy sixteen years old see Richey, De W. G., Arch. Int. Med., 1923, 31, 232.—*Translator*]; quite rarely from aneurysms of the coronary artery, (lit. Auffermann, Sommer), or of the pulmonary artery, or from rupture of an atheromatous coronary artery, and very rarely from a coronary vein (Pepere); (*c*) from trauma such as bullet and stab wounds of the pericardium and also the epicardium, (thus the author saw death after injury to a vein), but especially of the heart itself; from other forms of trauma, traumatic cardiac rupture with direct injury, bone fracture or compression; or in true rupture, either from internal pressure or tearing (Revenstorf, Bernstein, lit., Neue, Jaffe). The blood coagulates quickly or remains fluid, and 250 cc.–300 cc. suffice as a rule to cause death from tamponade of the pericardium, with the tension it causes whether by heart compression (Rehn) and the consequent prevention of diastolic expansion, or, analogous to the oil tension experiments of Cohnheim, from prevention of the emptying of the cavae in the auricles. As an exception, with a very powerful heart muscle, one litre may be found. The time of death depends on the kind of opening through which the blood escapes. In a large spontaneous rupture, death is sudden from paralysis of the heart, also in rupture from compression. In other cases of spontaneous rupture, death results later, perhaps after hours and even after days, if the tear is completed only after later enlargement (Ebbinghaus).

**Translator's Remarks.**—Thus in a 62 year-old woman, death occurred thirty-six hours after an initial and very severe pain. A cardiac aneurysm ruptured, and at autopsy 500 cc. of blood were found in the pericardial sac.

In stab wounds, and even more so in those prognostically unfavorable bullet wounds, this is often the case. The injured person can carry out complicated actions, defend himself, etc., a fact of great medico-legal importance (Ehrenroth). There is often time for satisfactory surgical treatment (Goebell, Borchardt, lit., Beck, lit., Luxemburg, Hesse, B. Fischer, Geringer, Hofmann, H. W. Gierke, Meyer-Pantin). Cases of perforating bullet wounds of the heart with heart tamponade without perforation of the parietal layer of the pericardium are described by De Josselin de Jonge, lit.

Traumata may be followed by inflammatory changes—pericarditis—especially if the pointed instruments such as needles, etc. are unclean. The author saw a case of suicidal intent in which a needle had been forced through the sternum, causing hemorrhage into the pericardium, accompanied by fibrinous pericarditis. Death resulted in a few days. The right ventricle during its movements, scratched its surface on the almost immovable needle, and thus arose the hemorrhage.

Small hemorrhages—ecchymoses—into the pericardial and subepicardial tissue especially on the posterior wall towards the base are seen frequently in asphyxia, especially in the newborn in whom the posterior coronary sulcus is chiefly the place affected, but there are usually hemorrhages into the pleura, thymus, etc., with severe agonal dyspnea. They are also found in poisoning (phosphorus), in septic infections (osteomyelitis), in hemorrhagic diatheses, in blood diseases, leukemia, pernicious anemia, and in eclampsia. They may appear as slate colored to black pigment spots, rarely nodules, and very rarely diffuse black discolorations of the parietal pericardial surface, (Borst). (Compare also subendocardial hemorrhages, p. 21.)

By applying, experimentally, relatively slight force to the thorax, Kulbs induced traumatic ecchymoses and hemorrhages into the valves and muscle.

Anthracosis may also be responsible for brown or black spots in the pericardium, brought there through the lymph channels from anthracotic bronchial and mediastinal lymph nodes. An actual evacuation into the cavity and rubbing into the epicardium must be very rare (Askanazy).

### Pneumopericardium

Air or gases are found very rarely in the pericardial cavity. They may enter through an osophageal rupture (trauma, foreign body, cancer), or

from the stomach, (cancer or simple ulcer), more rarely from the lungs or the pleura, (cavities, pneumothorax). Wounds from without penetrating the pericardium can allow entrance. Decomposition of exudates may produce gases. The term pneumotosis pericardii should be used only if the interstices of the pericardial tissue are filled with gas bubbles.

### Inflammation of the Pericardium. Pericarditis

The different anatomical forms are determined by the kind of exudate; thus there are differentiated:

#### Serous and Fibrinous, or Sero-fibrinous Pericarditis

A pure serous pericarditis, the exudate of which differs from the transudate of hydrops by its greater content of albumen, higher specific gravity and greater coagulability, does not remain for any length of time, but changes quickly to a sero-fibrinous pericarditis. After a preceding inflammatory hyperemia, dilatation and increased permeability of the pericardial vessels, the surface is coated with an albuminous fluid containing lymphocytes and isolated leukocytes and from which fibrin is deposited in granular form or as minute fibrils often interlacing, or as a substance of fine fibres, or as a homogeneous deposit. In the beginning the process is usually circumscribed.

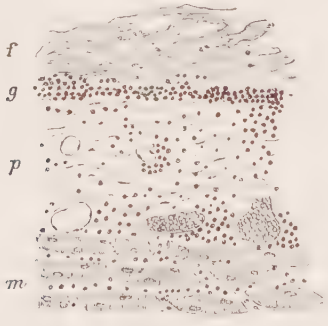



Fig. 1.

Fig. 2.

Fig. 1.—Pericarditis, fibrinous acute; m, heart muscle fibers; p, pericardial connective tissue with blood vessels and elastic fibers in which is cellular infiltration, especially marked at the boundary, g; above f, fibrin deposit; above g, lining cells are absent.

Fig. 2.—Fibrinous productive pericarditis; granulation tissue G, rich in vessels and young cells penetrates the fibrin f, which has been deposited on the surface in new layers; med. magn.

The serous layer loses its mirror-like gloss, a sure sign of serous inflammation. The pericardium suggests a pane of ground glass; after rubbing the back of a knife over the epicardium, it is dry, suffers an alteration of its

surface, the cellular coating is soon lost and it is covered with a veil of fibrin.

The covering cells are exfoliated after swelling and granular or fatty degeneration, or they lose their nuclei and undergo necrosis. There are gaps, and between the cells are fine fibres or broader strands of fibrin extending upward and loosening the cells. Finally the fibrin is directly attached to the connective and elastic tissues below. In early cases, there are still well preserved endothelial cells here and there on top of the fibrin, indeed to a small degree there are evidences of reproduction and regeneration. In other areas, the cells are covered by the fibrin membrane. In the pericardial vessels also, from which, naturally, the exudate has come, there may be a fibrin network or collections of leukocytes. Sometimes there is fibrinous exudate in the upper layers of the serosa itself.

The exudate, somewhat turbid from the admixture of leukocytes and desquamated surface cells, is usually yellow in color or red from slight hemorrhages and may contain free fibrin flakes. Its quantity varies and may reach one litre. In other cases it is so small that the term pericarditis fibrinosa sicca is used.

The fibrin often precedes the appearance of the serous exudation. If the serum is reabsorbed, the fibrin may remain. Thus are explained the remarkable changes in the clinical symptoms, friction, its disappearance and its recurrence.

If the coating of fibrin is thin, the markedly filled red pericardial vessels can be seen shining through in the vicinity of hemorrhages. In its fresh state, the membrane may be rubbed off by a knife and the mirror-like smooth serosa reappears. If the layers are plastered close on top of each other, especially the case on the visceral layer, the landmarks of the heart are more or less effaced. If the heart is covered by fibrin masses of light grayish yellow, or grayish red especially in the deeper layers from admixture of blood, and if it is like a network, or is furry, like a coat of sheep skin, it is called cor villosum or bread-and-butter heart. The fibrin masses first feel tough and somewhat rough but later become soft and friable.

The deeper layers of the pericardium in contact with the muscle are always hyperemic and show small round cell infiltration; the endothelial cells of blood and lymph vessels are enlarged.

Sometimes the fibrin masses are arranged as fringed masses over the left ventricle, especially at the apex, while on the edge of the right ventricle they appear as though combed. These latter are often approximately in parallel bands arranged at right angles to the long axis of the ventricle. On the part of the ventricle nearest the auricle, and above the conus pulmonalis, *i.e.*, on those parts which move the least during heart

action, the fibrin is deposited as a thick network or in honey comb layers. In the cases of dry fibrinous inflammation, the surfaces adhere and become displaced, so that the formation of typical figures can hardly take place. These develop best when there is much fluid and adherence of the pericardial walls is impossible, at least, over the more movable parts of the heart. The explanation of this peculiar arrangement lies in the continuous, regular and extensive movements of the heart muscle, especially during its contraction. In this way the fibrin masses deposited on the heart are pushed together in ridges as we see them on the right ventricle, while in other places, the fibrinous adhesions on the parietal pericardium are constantly torn apart again and fringes are formed especially at the apex. On the parietal layer these figures do not form typically.

### Further Course of Fibrinous Pericarditis

(*a*) **Absorption.** *Healing.*—The pericarditis may remain as described and then regress. The stiff exudate softens and breaks down into a granular detritus rich in fat droplets, and thus can be absorbed, but is also partly taken up by leukocytes and carried off (fat granule cells). Hyperemia disappears, the surface cells regenerate from those left behind and everything returns to normal. The softer the exudate, the quicker the pericarditis disappears, sometimes even in 24 hours, but usually the process takes place as in (*b*).

(*b*) **Organization of the Exudate by Productive Pericarditis** (*Fibrinous Productive Pericarditis*).—If the inflammation does not subside quickly, it assumes a productive character. Doubtless, the fibrin exerts a chemotactic effect on the connective tissue cells and blood vessels of the pericardium beneath. This leads to the production of a vascular granulation tissue from the connective tissue parts of the pericardial vessels which lifts the fibrin upwards. Or, more usually, the young tissue, rich in ameboid cells and budding vessels, penetrates the elastic border membrane and grows into the gaps between the fibrin masses which are more and more surrounded and broken up; they are then absorbed and the mass of fibrin is reduced to small islands. All of these processes take place in the course of a few weeks. Later, this granulation tissue in which the polymorphonuclear leukocytes are more and more reduced in numbers, changes into connective tissue and finally to scar tissue, poor in cells and vessels. Thus the healing process is concluded.

The gaps in the fibrin, or the spaces between the old and the newly formed tissue, or within the latter, may be lined with enlarged cubical surface cells on which fibrin perhaps exerted a stimulating effect and thus duct-like structures are formed (comp. p. 13, lit.), and Lauche saw cysts suspended like drops from the heart and lined with surface cells.

The growth of the granulating pericardium into the fibrin soon makes it impossible to pull off the deeper layers of fibrin.

## Generalities about Granulation Tissue and Its Change into Connective Tissue

Granulation tissue consists (1) of thin walled blood capillaries formed in great numbers by budding from older vessels; and (2) of a germinal tissue consisting of ameboid cells of diverse shapes; the former arise first as thick cellular outgrowths or buds of endothelial cells which become canalized and carry blood, the endothelial cells being distinguished by marked staining properties and the size of their nuclei. The germinal tissue contains: (*a*) as essential elements, young connective tissue and granulation cells, also called formative cells or fibroblasts (E. Neumann, Ziegler). They are produced by growth from fixed connective tissue cells —karyokinetic figures—are larger than leukocytes and show rounded or epithelium-like angular (epithelioid) or club-like, or many branched, but particularly spindle shaped forms with large, vesicular, light staining nuclei often with several nucleoli. Rounded polygonal descendants of the proliferating connective tissue cells are often found as energetic phagocytes with large nuclei, especially as the so-called pus phagocytes in purulent membranes; their protoplasm is foamy and often contains doubly refracting cholesterin derivatives, when they are called pseudo-xanthoma cells. But such macrophages may also come from lymphocytes (see Krompecher). (*b*) Lymphocytes. Lymphocytes are the cells which lie isolated in every normal, vascular connective tissue and which, with their derivatives, the plasma cells, produce the so-called small cell infiltration encountered in chronic inflammations in interstitial tissue, especially in the neighborhood of vessels, particularly veins. Their sources are partly from blood and lymph vessels and their capacity to wander is proven (emi- and immigration, see under tonsils), (Naegeli, Almkvist, Proescher, Schridde). They are also said to be derived from the preformed small lymph nodules of the organs (Ribbert) or by heaping up and local multiplication of the indifferent wandering cell of the connective tissue which is distributed everywhere, or from adventitial cells. ("Small ameboid wandering cells," Maximow.) They are small, but slightly larger than erythrocytes, rounded, uninuclear, very poor in protoplasm so that the hardly perceptible cell body surrounds the small, round, intensively staining nucleus like a pale ring. From these lymphoid cells, according to the accepted opinion, are derived the plasma cells or plasmocytes (see Marchand, Porcile, Martinotti). They have basophilic protoplasm and vacuoles, and are differentiated into those with young nuclei (lymphoplastic), with normal nuclei, (lymphatic) and with "spokes of a wheel"

nuclei, the latter being larger oval cells with eccentrically placed nuelci; the peripheral chromatin of the nucleus stains dark blue with methylene blue and bluish green with methyl green (wheel nucleus) while the protoplasm surrounding, is light, finely grained or grumous, (Marschalko). They also wander in the tissues. According to Unna (lit.), plasma cells are formed from modified connective tissue cells of every kind and not only from adventitial cells. They can degenerate by vacuolation (foam cells) or hyalinization (hyalin or Russel's fuchsinophile bodies). (*c*) The third types of cells are large round cells with relatively small, lightly stained nuclei and finely granular or vacuolated protoplasm. They are pronounced phagocytes (macrophages of Metschnikoff) and may contain, among other things, smaller cells (lympho- or leukocytes). Marchand calls them large mononuclear wandering cells (macrophages), and classes them among the so-called leuko- or better, lymphocytic cells which, as a whole, have their source in indifferent cells of the adventitia of capillaries and small veins. These are Maximow's so-called resting wandering cells, or Ranvier's clasmatocytes which, according to Ranvier, are leukocytes which wander from the vessels and become perivascular and sessile, and which may change into delicate long cells with rounded or elongated nuclei and prolongations of cytoplasm. These may further differentiate into lymphocytes and plasma cells, into mononuclear leukocytes or into these macrophages or even into giant cells (see also Herzog). Maximow speaks of polyblasts which he believes develop only during inflammations from both wandering lymphocytes, and resting wandering cells. Marchand thinks they are similar to the common wandering cells so generally present in the connective tissues and of about the same significance as its lymphocytes. Goldmann considers the pyrrhol cells which store blue pigment in their granules after intravital pyrrholin injections, identical with connective tissue wandering cells. Mobilized reticulum cells and endothelial cells (histiocytes, see under blood and spleen), are also supposed to belong to the mononuclear macrophages, (see monocytes of blood, and comp. Aschoff-Kiyono). (*d*) The fourth group are the leucocytes, polymorphonuclear or with multiple nuclei; well staining cells which wander from the blood vessels and appear in varying numbers and groups of different sizes in close proximity to vessels. They are also found heaped up in the lumena of blood vessels in the youngest parts of the granulation tissue. The histiogenic mast cells must be differentiated from the blood basophiles; according to Staemmler, they are unicellular glandular organs of connective tissue which furnish the necessary mucin required for the formation of interfibrillary cement substances. They usually occur in small numbers while occasionally eosinophilic leucocytes appear in greater numbers. Giant cells are much less frequent; they contain many nuclei,

are merely large granulation cells or are derived from blood vessel endothelium or from leucocytic cells (see above, under *c*). As foreign body giant cells, they serve to remove material difficult of absorption. It is of diagnostic importance to differentiate them from the giant cells of Langhans, (see under tuberculosis).

During the change of granulation tissue into fibrillar connective tissue the polymorphonuclear leucocytes as well as the lymphocytes gradually disappear. But the large connective tissue cells increase in number; in their protoplasm, fibrillae differentiate, fringes of fibres, bands and bundles of fibrillae form, while the cell bodies become fainter, and it might be thought that between the cells was formed at first a homogeneous interstitial substance from which later wave-like fibrillae differentiate, but Marchand assumes that the fibrillae of the ground substance have the same origin as the bundles. In this way the transformation to cicatricial tissue progresses until the whole consists of a firm fibrous background in which shrunken cells repose within the tissue spaces. These small cells, often with long nuclei, remain as fixed connective tissue cells which hug the fibrillar bundles closely. The older the scar tissue, the more the fibrous bundles predominate, while cells and vessels are very sparse; scar tissue hardens and contracts from shortening of the fibres.

If this vascular granulation tissue grows into the fibrinous masses from both sides, the two surfaces of the pericardium become adherent by broad flat, (sometimes only by small) fibrinous bundles, and a connected organized mass consisting of vascular granulation tissue which replaces the disappearing fibrinous adhesions (adherent pericarditis). The free surfaces of the membranes become covered with surface cells.

Adhesions from fibrinous exudation is an essential preliminary to obliteration of the space or parts. This applies to all serous membranes.

If, after disappearance of the fibrinous exudate, the productive fibrinous pericarditis is ended and healing takes place, the granulation tissue becomes connective tissue which in time becomes poor in vessels and shrinks.

During this process, the organizing fringes may change to polypoid or fringed fibrous nodules, and the non-adherent parts of the surface may show fibrous thickenings; rarely there forms a thick coating (zuckerguss), (Eichhorst) which the author has seen covering various abdominal organs (liver, spleen, etc.). Surfaces which were adherent may unite through spotted laminated adhesions or fibrous bands and cords stretched by the motion of the heart.

According to the degree, there are partial, but sometimes total, fibrous synechiae of the pericardial surfaces. If the pericardial cavity is thereby obliterated, it is called obliterating pericarditis.

Pericardial adhesions occur much less frequently than those of the pleura.

Partial synechiae appear most frequently as relaxed, small threads or bands with broad bases inserted on the cardiac surface near its apex or close to the base. When there is complete obliteration, the growth usually consists of the connective tissue arranged in layers with sufficient looseness to allow of their displacement. Even if the adhesions are short and tense and the pericardium is callous and thickened—fibropericarditis—or if there is complete inseparable coalescence of surfaces—which of course is usually not the case in rheumatic and simple infectious forms of pericarditis but only in tuberculous types—the heart action, its motility and especially its contractility can still be comparatively free, particularly if a well developed subserous fat deposit underneath the epicardium supplies a comparatively movable layer. But if this movability is absent, even when the adhesions are localized (Achelis), the adhesions themselves become clinically noteworthy from a systolic pulling in at the region of the apex (comp. Erben).

**Consequences.**—There is often secondary involvement of the myocardium; both ventricles become hypertrophic especially the left, (Wideroe) or, contrariwise, the muscle atrophies or undergoes fatty degeneration; the cavities then enlarge, often only in the right heart, and severe circulatory disturbances manifest themselves. Rarely is the myocardium intact. In marked chronic exudation, the myocardium, especially its surface layers, shows fatty degeneration; if this causes decompensation, congestive symptoms develop leading to hydrops. The left lung may be compressed by a large pericardial exudate and thus be emptied of air.

**Cicatricial Mediastino-pericarditis.**— When a pericarditis extends through to the outer surface of the pericardium—pericarditis externa—the cellular mediastinal tissue may become involved in the exudative process and later cicatrization. This may interfere with the blood flow in the large vessels, clinically shown by pulsus paradoxus, (Kussmaul), and inspiratory swelling and diastolic collapse in the veins of the neck. Wenckebach calls attention to an inspiratory pulling in of the lower sternal angle and its vicinity, instead of the normal lifting movement.

Cicatricial change in a productive pericarditis on areas free from adhesions leads to the formation of diffuse icing-like, or circumscribed veil-like thickenings called tendon spots, macula tendinea sive lactea, or soldier's spots.

Under this term are considered two separate changes, not always easy to differentiate:

(*a*) Those, the result of a productive pericarditis, a localized pericardial fibrosis. These white thickenings readily testify to their inflamma-

tory origin, if the surface shows thread-like, fringy or small nodular connective tissue outgrowths, *i.e.*, if they are rough and uneven, but if they are smooth, they may be mistaken for simple pericardial scars. They often appear on both surfaces.

(*b*) Simple peri- and epicardial scars of non-inflammatory origin and consisting of sclerotic connective tissue poor in cells are very frequent and found in about 80% of cadavers, particularly, and regularly in old people. They may appear on both surfaces, but this is unusual. Generally they are located anteriorly on the right ventricle on the conus of the pulmonary artery, but may also be found on the posterior surface of the ventricles, in areas where the pericardium covers the large vessels, where the vena cava enters, and at the branchings of the coronary arteries. They are smooth, white, satiny thickenings of the pericardium often angular, sometimes rounded or oval, usually well circumscribed, either thin and transparent or thick, firm and tendonous, and often laid down like a

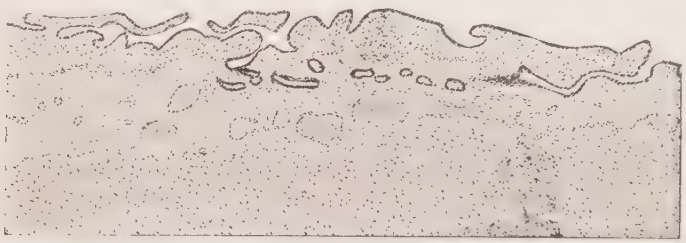


FIG. 3.—Pericardial milk spot with gland-like proliferation of cubical lining cells; low magn.

plateau; they may reach the size of a silver dollar or more. They sometimes appear as small nodules. Probably the form most frequently met is from mechanical causes (Friedreich), such as pulling, friction, and pressure, from heart action, and are then callous work hypertrophies with degeneration from hyalin and sclerotic changes without increase in elastic fibres as in scars. Herxheimer assumes they arise from primary mechanical lesions of the surface cells (comp. also Tsunoda). This explanation does not satisfy in some cases, *e.g.*, in small children; Czerny thinks they are the remains of adhesions with the amnion, (amnion spots); Ribbert supposes they result from disturbances in the separation of the leaves of the pericardium.

Microscopically, the connective tissue layers may include dainty gland or duct-like formations and spaces lined with cubical cells which originate from the surface cells, (comp. p. 8). (See R. Meyer, Ribbert, Tsunoda, Tsiwidis.)

Petrification results if lime salts are deposited in larger quantity which occurs relatively seldom. (The cheesy and fibrinous masses in tuberculo-

sis may calcify and the heart be surrounded more or less by flat or spiky lime deposits in a broad ring or armor—petrified heart.)

Clinical signs may be absent.

We have rarely seen extensive changes of this sort. True ossification of the pericardium is also rare.

(*c*) **Chronic Productive Pericarditis.**—Although every productive pericarditis following fibrinous exudation is chronic in a certain sense on account of the slow healing which extends over weeks, the inflammatory process nevertheless has a reparatory character since it absorbs and replaces the exudate. Productive inflammation becomes truly chronic—a chronic fibrinous productive pericarditis—when new fibrinous exudate is continuously deposited while the granulation tissue from beneath penetrates and replaces it and slowly and continuously changes to connective tissue. In this way, the pericardium becomes much thickened, up to 0.5 cm. and often over its entire surface.

If a new fibrino-exudative process occurs after the conclusion of one inflammatory process, it is called recurrent fibrinous pericarditis.

Anatomically this can be diagnosed quite accurately by finding new fibrin deposits on a scarred thickened pericardium with absence of cellular granulation tissue.

In rare cases, no adhesions occur, but there is marked shrinking of the whole heart.

### Purulent, Suppurative and Ichorous Pericarditis

The first may occur alone or combined with sero-fibrinous pericarditis; in the latter case the fibrin masses are smeary, soft, and half dissolved. A true purulent exudate is creamy, thick, yellowish green, and consists of albuminous fluid plus enormous masses of pus cells, the polymorphonuclear leucocytes predominating.

Rarely, we see not only purulent exudation on the free surface, but also partial suppurative tissue destruction of the pericardium itself.

If healing by absorption or death does not occur soon, a productive inflammation quickly develops with the pericardium resembling a "pyogenic membrane," containing pus phagocytes, (comp. p. 9). If this condition has persisted for some time, we find the pericardium remarkably large and thinned, or perhaps thickened by fibrous tissue; if many adhesions form, the pericardial cavity shrinks and finally is obliterated.

The exudate, even if plentiful (up to 1 litre), can undergo fatty degeneration and be reabsorbed, although slowly; occasionally it thickens like cheese and calcifies and then shows lumpy, chalky or plate-like, hard as bone, masses between the adhesions (do not mistake for tuberculosis).

Purulent pericarditis often invades the neighboring structures, especially the cellular tissue of the mediastinum, and sometimes the myocardium also. From purulent pericarditis may develop through decomposition, an ichorous fluid, greenish, foul and filled with gas bubbles.

**Results.**—Purulent, ichorous pericarditis is very grave. Death may ensue from paralysis of the heart which occurs, not rarely, from fatty degeneration of the myocardium; in other cases which end quickly in death, an inflammatory edema of the myocardium is the cause.

### Etiology of Fibrinous, Purulent and Fibrino-purulent Pericarditis

Pericarditis in most cases is secondary, usually hematogenous in origin from some focus in another part of the body. It occurs most frequently in infectious diseases, particularly acute articular rheumatism which usually includes the endocardium also. Nenninger found cardiac complications in 60% of the cases of articular rheumatism, (see also under joints). But pericarditis does appear, although more rarely, in other infectious diseases such as scarlet fever, measles, small pox, cholera and even gonorrhea. It is relatively frequent in chronic nephritis, chronic alcoholism, and other cachexias.

It is a question in nephritic pericarditis whether there is not a peculiar predisposition on the part of the pericardium to harbor microorganisms, or whether it is occasionally due to a purely toxemic (uremic) cause without bacterial activity (Banti). In uremic pericarditis, Marchand-Herzog found a remarkable proliferation and desquamation of the surface cells between the fibrinous membranes while leucocytes as well as lymphocytes were almost entirely absent (compare under endocarditis p. 37).

The suppurative variety is less frequent than the sero-fibrinous, and develops by metastasis especially from severe pyemic processes such as puerperal fever. The author has seen this form arise from circumscribed phlegmons in connection with felons, or furuncles or tonsillar abscesses; occasionally it is seen in articular rheumatism and in chronic nephritis.

In other cases it results from contiguity, (*b*) *i.e.*, from disease of the myocardium—abscess, tumor, chronic myocarditis—from the endocardium, or from neighboring structures.

This means from inflammations of the pleura or lungs, inflammatory processes, mostly purulent or ichoric, of the esophagus—carcinomatous invasion or foreign body phlegmons—from the bronchial or mediastinal lymph nodes, from mediastinal tissue, caries of vertebrae or ribs, from the stomach, liver or peritoneum. All such inflammatory processes in the pericardium are fibrinous at the start.

The most important bacteria are staphylococci, streptococcus pyogenes and diplococcus lanceolatus (pneumoniae).

Traumatic (*c*) causes include stab and bullet wounds, perforation by a foreign body from the esophagus, blunt traumata such as blows, or pressure. Doubtless, subcutaneous lesions produce a point of lowered resistance which permits bacteria circulating in the blood to become established and produce pathogenic effects. But there are also traumatic pericarditides, usually fibrinous, without bacteria (lit. Stern, Kulbs, and others).

### Hemorrhagic Pericarditis

Blood may be mixed with the fibrinous exudate, or the exudate of 1.5 litres or more is sometimes almost pure blood.

This is seldom found in the ordinary infectious diseases, but is quite frequent in tuberculous pericarditis, in secondary tumors—carcinoma, more rarely with sarcoma—in Bright's disease and where there is a tendency to hemorrhage such as in hemophilia, purpura, scurvy, etc.

## Infectious Granulation Tumors of the Pericardium

These are inflammatory new tissue growths which develop under the influence of specific infectious microorganisms. The product is granulation tissue (comp. p. 9) or granulomatous tissue, which has a specific pathological character depending on the respective organisms; since it appears as small or larger nodules, it is somewhat similar to true tumors (neoplasms).

1. Tuberculosis is almost always secondary to a tuberculous lesion elsewhere. There are differentiated: (*a*) miliary tuberculosis (tuberculous pericarditis) in which small nodules containing tubercle bacilli appear, often along the vessels of the pericardium, which is otherwise unchanged. Very similar nodules may be composed of carcinoma cells, or more rarely of amyloid. This form is less frequent than (*b*) Pericarditis tuberculosa which is probably the most common form of chronic sero-fibrinous, or fibrino-hemorrhagic, more rarely fibrino-purulent inflammation, and is differentiated from simple chronic pericarditis by the presence of numerous tubercles.

Quite frequently, a hemorrhagic, or pure bloody, exudate amounting to several litres is present although the author saw a simple serofibrinous exudate up to 2 litres. The tubercles are of lymphoid or giant cell type, discrete, or fused, lying in vascular, overgrown young tissue. They may coalesce into cheesy material forming thick, whitish yellow layers in the grayish red granulation tissue (cheesy pericarditis).

Scratch the superimposed fibrin layers and observe carefully the section surface to see the tubercles. Often, they are only found micro-

scopically, some between the fibrin, and some in the thickened pericardial tissue.

Regarding the forms of "pearl disease," resembling the bovine tuberculosis of animals, see under peritoneum.

In chronic tuberculous pericarditis, the pericardium, especially the visceral layers, may be thickened to 1 cm. or more.

Pericardial adhesions are very frequent, but usually less firm than those of simple chronic pericarditis, because of caseous degeneration. Calcification, see p. 13.

**Cause.**—Miliary tuberculous pericarditis may be hematogenous but usually, like tuberculous pericarditis, is lymphogenous in origin from tuberculous processes in the vicinity –lungs, pleura, lymph nodes, especially those in the anterior mediastinum.

2. Syphilis in a gummatous calloused form is rare. A granulating, scarring pericarditis may arise over gummatous nodules in the heart muscle, and may lead to firm adhesions of the pericardial surfaces.

3. Actinomycosis is usually induced by invasion from the mediastinum, from a cervical or a pulmonary lesion. In typical cases, it appears as fibrous adhesions between the pericardial layers, pleura and mediastinal tissues. In the calloused masses are cavities and fistulous tracts with yellow purulent, or jelly-like, contents which contain the peculiar colonies of actinomyces as minute sulphur granules, sometimes in immense quantities. Actinomycotic granulations are known to have penetrated the myocardium and entered the cavities and vessels of the heart.

A rare preparation in the museum at Basle (published by Munch) shows actinomycosis invading the mediastinum and pericardium from the lung, and penetrating the cavity of the right ventricle, also the large coronary vein. From the left auricle, fragments of a decomposing nodule the size of a bean, caused a generalized actinomycosis, with numerous metastases in distant muscles (arms and legs), in the skin (in the extremities and the head), in the intestines, kidneys and in one testicle (compare cases of Schmorl, Paetzold).

### True Tumors

Primary tumors of the pericardium are quite rare. In a dye worker, 35 years of age, who had chronic verrucose endocarditis, the author saw within the thickened pericardium, which was filled by 400 cc. of serofibrinous hemorrhagic exudate, three flaccid edematous fibrous polyps with broad pedicles. Two were located on the posterior wall, and one showed finger-like branching; the third, the size of an apple, grew anteriorly (comp. Jarisch).

One lipoma each, is mentioned by McKechnie and Struppler. The author saw a finely fibrous, pedunculated lipoma, with smooth tendon white coating almost ready to become a loose body (corpus librium); and another the size of a chestnut, suspended from the posterior wall of the left ventricle, which continued in the musculature as far as the atrioventricular insertion of the posterior mitral valve leaflet. In very rare cases (Klob, lit.), in pericardial lipomatosis, fat masses may tear free of their pedicles and become laminated "free bodies" (see peritoneum). The "corpora libra" in the pericardium are mostly hyalinized and smoothed fibrin clumps, or torn off, organized fibrin masses. They may also calcify (quite rare). Sarcomas are mentioned by Drysdale, Kaak, Tobiesen, lit. Dietrich mentions a papillary carcinoma which he thinks was derived from the surface cells.

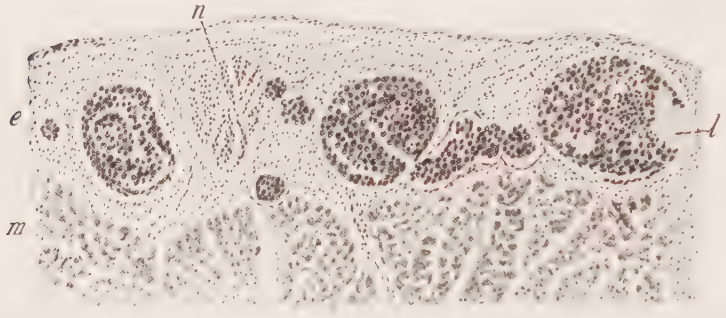



FIG. 4.—Extension of carcinoma in lymph vessels of the epicardium (carcinoma of esophagus); m, myocardium; e, cellular epicardium; n, nerve; l, lymph vessels filled with carcinoma plugs; × 56.

Carcinomata and sarcomata are seen as secondary tumors from the vicinity or metastatic to some distant primary focus. Sometimes, carcinoma infiltration is masked by its resemblance to a soldier's spot on the epicardium, and is recognized only microscopically. If rapid invasion of a diffuse or nodular type takes place, inflammation, usually mild, is initiated (carcinomatous pericarditis). Sarcomata, especially lymphosarcomata derived from cervical or mediastinal lymph nodes, produce at times a very thick, diffuse, board-like infiltration of the pericardium, especially of the parietal layer and the parts of the visceral layers resting on the auricles. Carcinoma of the esophagus, the bronchi, or the stomach may occasionally produce the same results through the lymphatics.

Of parasites, it may be said that occasionally cysticercus, trichina and echinococcus occur.

### Changes in the Pericardial Fat

There are (*a*) hypertrophic, (*b*) atrophic conditions.

(*a*) Increase of pericardial fat (fatty heart) may reach a high degree leading to lobulated fat deposits sometimes as thick as a thumb, especially in obese individuals. The regions of choice are at the edge of the right ventricle, the area about the conus pulmonalis, the rim of the left ventricle, and the apex. Because the fat penetrates the muscle bundles, the subsequent atrophy of the muscle has great clinical importance.

(*b*) So-called mucous, or better, serous, or gelatinous atrophy of fatty tissue is frequently found in emaciated, cachectic, senile, carcinomatous, or phthisical individuals. The yellow fat is changed to a jelly-like brown substance. It is caused by atrophy of fat cells and an accumulation of edema fluid in the spaces left by the tissue destruction. The fat cells, after coalescence of the fat droplets into globules, revert into variously shaped connective tissue cells,—rounded, spindle, stellate—which lie in an edematous ground substance and contain fat globules of yellowish brown color. These cells may shrink so that they finally correspond to common connective tissue cells.

## ENDOCARDIUM

The endocardium consists of a layer of thin fibrous and elastic tissue with smooth muscle fibres, the latter especially at the conus arteriosus (Nagayo), the whole covered with endothelial cells. Between this and the heart muscle is the loose, fibrous subendocardial tissue connected with the intermuscular connective tissue of the heart itself. The valves are rich in elastic fibres.

With Browicz, we differentiate several types of tendonous fibres: (*a*) valvular, which are constant, (*b*) parietal, inconstant, (pseudo), in contact with the muscle trabeculae and against the walls, (*c*) intraventricular (pseudo), suspended within the ventricular cavity, and according to Huchard, if they vibrate, the cause of abnormal sounds. Besides those in the ventricles, they may be present in the right and left auricles, (see under cardiac malformations). [So-called Chiari's network is a system of coarse to fine fibres in the right auricle probably as a congenital anomaly. See Jordan, W. R., Arch. Path., 1926, 2, 841.—*Translator.*]

Certain tendon-like formations of the ventricle resembling the types (*b*) and (*c*) are considered by Tawara and Magnus-Alsleben as anomalies of the atrioventricular muscle fibre system (Tawara's conducting system). Moenckeberg accepts Tawara's explanation for only certain of the so-called pseudo-tendon fibres, *i.e.*, those which contain Purkinje fibres (proof by

glycogen staining) and not for others which contain only ordinary heart musculature, or none at all (lit. by Herxheimer and Thorel).

The muscular and neuro-muscular atrioventricular system is considered by its discoverer as the sole muscular connection between auricles and ventricles, (bundle of His). However, since its function is to conduct stimuli from the auricle to the ventricle (papillary muscle area), it has been called the conducting system. It begins, according to Tawara, on the right side of the auricular septum in the vicinity of the coronary vein and while still in the septum, forms a nodular thickening, Tawara's, or the atrioventricular node. Histologically, it is formed by fusion of two divisions, from an auricular and a ventricular node with their processes. It passes through the septum as His's atrioventricular bundle which also contains non-medullated nerve fibres, (Wilson, Engel, Oppenheimer) and is surrounded by numerous ganglion cells. It reaches below the pars membranacea to the base of the ventricular septum where the trunk (crus commune) divides into two branches, the left being the larger, which follow the septum downward, passing first through the trabeculae to the papillary muscles where they are distributed in both chambers predominantly as a subendothelial network. These fibres are analogous to Purkinje fibres of the horse, but have a firmer and more isolated connective tissue sheath which may be injected (Aagaard and Hall); the terminal prolongations which gradually lose their special structure—their cable-like isolation—by connective tissue, fat and lymph spaces, communicate by continuity with the ventricular muscle fibres. This conducting system which differs as to its fibres from the other heart muscle by its greater wealth of glycogen and sarcoplasm, is poor in fibrillae, lacks the cross striations, the step-like gradations, the anastomoses with neighboring cells, and is in a many-meshed net-like arrangement. A very generous blood supply to the system is furnished chiefly by the right coronary artery (Haas). At the anterior border between the superior vena cava and the rest of the right auricle, lies another nodule similar to the first named, the Keith-Flack, or sinus node (Koch). According to Thorel, this has a connection with the atrioventricular ganglion by means of the fibres of Purkinje; Kulbs succeeded in demonstrating such a specific connection of the muscles in animals, but it is still undetermined in man (comp. Hubert).

While Aschoff and his pupils searched for the point of origin of the stimulus for the conducting system on the anterior margin of the opening of the coronary vein, most others see the origin of normal heart action in the sinus node.

The afferent cardiac nerves, the vagus (moderator), and the nervus accelerans, end, for the most part, in ganglion cells from which nerve fibres

emerge and freely enmesh the muscle fibres. While ganglion cells are usually absent in the actual walls and in the ventricular septum, they are arranged in groups in the bundle of His, especially in the ganglion, and the left vagus supposedly influences the stimulation in the atrioventricular ganglion while the right vagus affects the sinus ganglion (comp. L. R. Muller, Glaser).

See Moenckeberg's complete references in the lit., also Tandler, in regard to the anatomy and physiology of the bundle of His; also see Monckeberg, lit., as to its development, and its characteristics in extensive cardiac malformations.

The functional importance of this system is clearly brought to our attention in the Adams-Stokes symptom-complex with its peculiar bradycardia due to heart block. In milder degree, the ventricles beat more slowly than the auricles; in complete dissociation (auriculo-ventricular block), the ventricles and auricles beat quite independently of each other, *i.e.*, the ventricular beat is no longer controlled by the rhythm of the auricles, when the conduction of the stimulus from the auricles to the ventricles is "blocked." In a number of these cases with fainting spells, etc., it has been proved that there is a break in the continuity of the bundle of His caused by scars, gummata, calcification, etc. (lit. by Monckeberg). But incomplete dissociation is possible when the bundle of His is intact anatomically, *e.g.*, in scarring processes of the musculature which ceases to react to the special stimuli (muscular type in contradistinction to transmission type). The cause of the neurogenous or Morgagni type is peripheral (vagus), or central (medulla oblongata), in the cardiac nerve apparatus (Nagayo, see Monckeberg). But to what extent diffuse or circumscribed pathological changes in the system such as adiposis, loss of glycogen, fatty degeneration, common, or so-called rheumatic nodular infiltrations, hemorrhages, etc., can be associated with cases of cardiac weakness or of sudden death by heart failure is still an open question. Loew and Sternberg believe there is little or no relationship.

Subendocardial hemorrhages have recently claimed attention. They are frequently observed, but must involve the bundle of His alone, especially its left side (Monckeberg, and others), and thereby be differentiated from the hemorrhages in asphyxia which usually affect both the endocardium and the pleura. They are found in infections (Sternberg), especially diphtheria (Berblinger, Zum Winkel), after the administration of certain cardiac drugs (Aschoff), in tetanus, eclampsia and other convulsive conditions (Ribbert). Vagus irritation seems to be of special importance because, either in consequence of its paralysis, or because of the effect of abnormal contractions of the left ventricle, there is congestion in the remarkably rich vascular system of the bundle which might lead to

mechanical capillary tears (comp. Berblinger, lit.). Nothing more definite is known of the pathological consequences of such hemorrhages, except that fibres of the bundle of His have been found degenerated within their confines.

The fact that under certain conditions the pathological changes are confined to the bundle of His, and under other conditions, more marked anatomical changes are noted in the bundle (Monckeberg), without suggestive symptoms during life, must compel reserve in the recognition of a special pathology of the bundle of His (Aschoff) in the expectation of perhaps a "newly evolved pathology of the heart on the basis of investigations of the bundle," (see Monckeberg, Wenckebach). Tendeloo only recently voices doubts as to whether marked changes of the bundle **per se** will directly cause cardiac insufficiency (other lit. in appendix).

### Vessels of the Valve Leaflets

In the soft and fleshy valves of the fetus, there are vessels, and in the auriculo-ventricular and the tricuspid valves of the newborn, they still reach to the free valve margins. In the adult, however, the auriculo-ventricular valves have vessels only towards their bases, but a productive endocarditis may bring about formation of many new vessels.

Fenestration between the margins and the free edges of the semilunar valves (lunulae) may be congenital, or occur in advanced age as a result of marked thinning—atrophic tissue loss, atrophy from inactivity,—but the author has seen it in youth also when there were congenitally large and tender valves. Beneke also speaks of atrophic fenestration. The edges of these oval or slit-like fenestra are smooth, differing from those of ulcerative processes by absence of infiltration and fibrous thickening. They cause no functional disturbances when linear holes are above the edge of closure especially when they are in the lateral part of the valves near the angles of insertion. Occasionally, quite tender auriculo-ventricular valves are also seen.

### Simple Degenerative Conditions of the Endocardium

(*a*) Fatty degeneration macroscopically takes the form of white or yellowish white spots appearing especially on the ventricular side of the anterior mitral leaflet; it occurs frequently in old people, but may also develop, even in children, in anemia, intoxications and infections, and is often combined with calcification.

Microscopically, some of the cells in the spaces between the connective tissue fibres are filled with minute droplets. The "white spots" on the ventricular side of the large anterior mitral leaflet are degenerations of the connective tissue to which accumulations of fat and lime, eventually also

cell growth, are added, (Beitzke). Some speak of this as "atherosclerosis" (Sato, lit., Anitschkow). Doubtless, mechanical factors play a part—injury of the valve during systole (see p. 42); according to Martius, (lit.), the action of poisons, infections, and also nutritional disturbances must be considered, especially in children (see experiments of Anitschkow).

(*b*) **Sclerosis.**—The endocardium becomes calloused, white, glassy and hyalinized (hyalin degeneration). Often an entire valve, especially the tricuspid, but sometimes only a portion at the free rim, is affected. The mural endocardium of the auricles and ventricles may show white spots and striae. A diffuse thickening is less frequent.

Hyalin degeneration is particularly prone to occur in places already changed by granulation tissue.

Microscopically, broad connective tissue fibres lie close together with very few cells between; the connective tissue, otherwise reticular, becomes compact, glassy and homogeneous.

(*c*) Mucoid softening consists of transformation of firm fibrous tissue to a gelatinous mass consisting of a mucoid background with more or less numerous embedded branching cells.

(*d*) **Calcification.**—Lime salt deposits (petrefaction), occur chiefly at the bases of sclerotic leaflets or those with fatty degeneration.

The lime salts are visible as grumous masses which stain deep blue with hematoxylin. That portion of the lime not visible is held in solution by protein colloids and carbonic acid in the blood and tissue fluids which saturate cells and tissues.

(*e*) Atheromatous degeneration consists of a soft necrotic disintegration of parts of the valve tissue which usually shows, in addition, the regressive changes just described. Quite frequently there is a combination of necrotic and fatty disintegration, (microscopically there is granular fatty detritus with cholesterin crystals).

(*f*) Amyloid degeneration is rare in its more advanced grades, in which the endocardial as well as the myocardial connective tissue contains macroscopic clumps and nodules of amyloid substance (Heschl, Ziegler, Wild, Beneke, Stumpf, lit.); as a rule, this change is then found in other organs also, and is rarely confined to the heart muscle (Landau); microscopically, mild forms are frequent (see Huebschmann, also pp. 41, 55). M. B. Schmidt found networks of lymph and blood vessels in the valves that were filled with amyloid material.

All the changes mentioned under (*a*) to (*e*) are especially frequent in advanced age, but are found in a milder form in earlier life also, (Moenckeberg). They affect chiefly the valves, often those that have undergone the changes that follow inflammatory processes, but may develop in the

mural endocardium of the ventricles and auricles, especially in the left. Sometimes special mechanical factors are at work; according to Zahn, friction from the blood stream is important, especially in insufficiency of the aortic valve, but pulling and pressure during opening and closing may account for the development and localization of these changes, especially those described under (*a*) and (*b*). In other cases, inflammatory residues are predisposing factors, especially those of cicatricial nature in infectious endocarditis, but the most frequent reasons are simple senile regressive changes which may appear prematurely in middle life as the result of overworked valves. A tendonous change in the papillary muscles, or of isolated chordae tendineae, (Loewenstein) is a sign of wearing out processes, (see Rossle), and is analogous to the calcification of the annulus fibrosus mentioned on page 41.

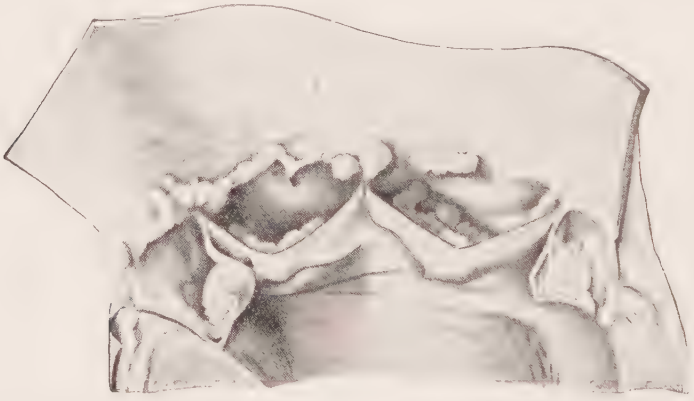


FIG. 5.—Aortic valve leaflet markedly sclerotic and calcified from an 85 year old man. Calcareous clumps deep within and at upper border of sinus of Valsalva; the valves rigid and almost immovable.

Progressive conditions, such as cartilage and bone formation in the valves, are seen much less frequently (comp. Rosenstein, Rohmer, see also Mebius, lit.).

When the degenerated or roughened areas are on the surface thrombosis may occur. The thrombus may be more or less organized by a productive inflammation, however inactive, which starts in the surrounding tissue of the endocardium.

If the process is often repeated, there result nodular or diffuse thickenings to which calcification is added.

Sclerosis and atheroma, thrombosis and calcification, rarely true ossification, produce exceedingly irregular thickenings and changes in form—sclerosis and atheroma of the valves. (See "non-inflammatory endocarditis" called by Dewitzky "thrombo-sclerosis," Felsenreich and von Wiesner, p. 42.)

Functional disturbances result just as they do in fibrosis of the valves following infectious endocarditis. Ofttimes it is not easy to decide whether a particular case is an infectious endocarditis or a primary sclerosis and atheroma. Quite exceptional difficulty is encountered because chronic fibrous thickening of the valves induces regressive tissue changes similar to those noted under (*a*)–(*e*).

**Differential Diagnosis.**—Usually, primary regressive changes are not sharply outlined; especially in the auriculo-ventricular valves, they are often plateau-like, or distributed flat over the whole apex to be lost without margins in the adjacent tissue. They do not elect the typical places of predilection of endocarditis (margins of closure). Thus we often see calcified layers or nodular excrescences in the aorta in the depths of the pockets of the otherwise almost unchanged leaflets, or at the points where the leaflets are attached to the aorta, or at the upper border of the sinus of Valsalva; these places are where the greatest tension and pulling occur from the backflow of the blood column during diastole. An endocarditis would not localize there, but in the ventricular direction and on the auriculo-ventricular valves, where the free edges and adjacent parts undergo diffuse thickening. We often see sclerosis of the aortic valves, also, together with sclerosis of the aorta; in this case, the process extends from the aorta to the leaflets, attacking especially the margins and extending outwards towards the valve base (see, among others, also differential diagnosis p. 40).

For more details in reference to normal and pathological histology of the parietal endocardium, see *Nagayo*, also page 43.

### Endocarditis. Inflammation of the Endocardium

If the term "endocarditis" is used alone, it means an infectious inflammation of the valves—valvular endocarditis. But there is also a ventricular or mural endocarditis which may localize anywhere on the inner walls of the heart. Endocarditis on the chordae tendineae is called chordal endocarditis.

Care must be taken not to confuse with signs of endocarditis, especially in decomposing bodies, the redness of the valves from blood pigment leaving the corpuscles, coloring the serum and saturating the valvular tissue; this is only a post mortem blood imbibition.

Several anatomical forms of endocarditis are described. To understand their points in common, we shall briefly sketch the origin of the inflammation of the endocardium, and how the several forms develop. We take for granted, at present, in the etiological consideration, that injurious factors to the endocardium are not uniform in nature. We shall touch upon this later. Injuries may be caused by bacteria with their

accompanying toxins, or by the toxins alone as they are evolved during infections, or likewise by any other toxic-chemical substances which are formed within the body during certain diseases that contaminate the blood—nephritis, diabetes, carcinoma, etc. We will consider the case in which endocardial inflammation is caused by bacteria circulating in the blood. What are the endocardial lesions and what are the reactive appearances? We assume that the bacteria are present in masses and form a fine, gray, granular coating on the endocardium. It is well to remember that these loosely placed masses may be easily wiped off by needless and careless manipulation of cardiac orifices during post mortem examination. The endothelium and eventually to a greater or less extent, the deeper layers of the valves undergo necrosis below this coating, and this primary change is more marked the more virulent the bacteria; their toxic products must be held directly responsible. The rapidly passing blood stream may tear off the bacteria and if the endothelium is not directly killed, it may show cloudiness, swelling and desquamation.

In certain infectious diseases such as scarlet fever, measles, etc., the cells may be stimulated to proliferation from exclusively toxic action causing intensive cell increases in the subendothelial and deeper layers; round cell infiltration and granulation tissue growth follow. Thrombi are absent in those cases in which the proliferating endocarditis is demonstrable only by the microscope (comp. Baldassari, Czirer).

Over the area deprived of endothelium, a thrombotic coating from the blood is formed which is composed chiefly of blood platelets, some fibrin and leucocytes, and some erythrocytes; this may also contain bacteria. The thrombi have the appearance of being coated with sand.

Because they consist chiefly of clumped platelets, which differentiates them from the white thrombi of the veins which are rich in fibrin and leucocytes, these thrombi are glassy, firm, and more securely attached to their bases. For this reason the blood current cannot tear them away or break them into fragments so easily.

Thrombus formation in endocarditis is secondary, and we might speak of endocardial thrombosis. Thrombo-endocarditis (Ziegler), a term used by some instead of endocarditis, leaves the relation of thrombi and endocarditis in uncertainty; it may be interpreted in a double sense, either an endocarditis added to thrombosis, or an endocarditis combined with thrombosis. We avoid this double meaning, also for the reason that thrombosis may be absent microscopically in highly infectious, as well as in certain proliferative inflammatory, perhaps toxigenous, forms of endocarditis (see Czirer, lit.).

The second phase of the endocarditis is now reached. Where there are vessels around the necrosis, a reactive inflammation sets in; where

vessels are absent, the fixed connective tissue cells in the valves multiply actively and leucocytes appear (productive proliferating inflammation). Later, vessels begin to penetrate. If the necrosis is progressive and intensive on account of numerous, or worse, highly virulent bacteria which actively penetrate the tissues, portions of the valves dissolve or become detached by active pus infiltration which spreads in the vicinity and softens the tissue. The course is subacute or chronic if the process is less intensive and less progressive, and then, in time, warty, or flat hyperplastic granulations appear on the valves.

The degree of connective tissue proliferation, naturally, is as varied as the kinds of causative factors. In non-bacterial endocarditis, the reaction is less severe than in the infectious variety.

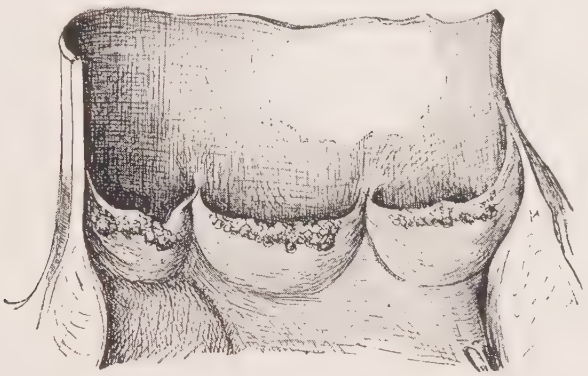


FIG. 6.—Verrucose endocarditis of the aortic valves in articular rheumatism.

Thus we see that endocarditis, like any other inflammation, is composed of these phenomena: (*a*) tissue changes which vary from stimulation, to active endothelial proliferation, (see p. 26), to very grave alterations, *i.e.*, necrosis; (*b*) exudation, and also (*c*) hyperplastic regenerative proliferation. Thrombus formation is accessory, and is conditioned by the special location of endocarditis. It is especially prone to occur in deeper endothelial, or endocardial lesions, as mentioned above; it is entirely absent in certain forms of productive endocarditis.

When there is quick destruction of valve tissue, it is called endocarditis ulcerosa or maligna; endocarditis verrucosa shows slight necrosis and is characterized by warty outgrowths of proliferating tissue.

Chronic fibroplastic, so-called fibrous endocarditis, (contracting endocarditis), is a chronic form distinguished by shrinking of the granulating valve tissue; it is often only a continuation of a vegetative endocarditis.

Accordingly we differentiate the following anatomical forms:

1. Vegetative, warty or verrucose endocarditis, (productive, simplex, rheumatic).

2. Ulcerative, malignant, necrosing, acute destructive endocarditis.

3. Chronic fibrous, fibroplastic, contracting endocarditis. Number 1 and 2, or all 3 forms may be combined.

The terms malignant and simplex are used here in an anatomical—not in a clinical—sense; the two conceptions are not identical. Clinically, the terms indicate the etiology and course of the disease, while anatomically the endocarditis found after fatal infections may be vegetative—*e.g.*, from pneumococcus septicemia, or ulcerative (malignant), (see Litten).

### Vegetative Endocarditis (Warty-simplex) (See Fig. 6)

Peculiar thrombotic precipitates are formed from the blood on the injured surfaces of the valves. If the endocarditis appears in infectious diseases with known agents, the corresponding organisms are found in the early stages in the necrosed surface layers and beneath the coating of the valves which points to the hematogenous route of infection. A productive inflammation, usually showing slight leucocytic infiltration of the endocardium, is seen in the vicinity of the platelet-covered surface necroses. The fixed cells of proliferating valve tissue appear enlarged and increased, and penetrate into the coating, replacing and organizing it from below (fig. 7). At this stage, bacteria can no longer be demonstrated. New blood vessels growing from the base of the valves form capillary networks which send prolongations into the organizing nodules. Leucocytes may emigrate from these vessels. In the beginning, the nodules are translucent, resembling the old fashioned "blotting sand," pale red, and gelatinous, but as the granulation tissue changes into connective tissue, they become more opaque, grayer or whiter, and the firmer they become, the firmer they adhere to the underlying tissues. Sometimes they resemble condylomata, polyps, or rooster's combs in consequence of the abundant fibrinous thrombotic deposits.

The first fresh coating may appear flat, like a serosa freshly coated with fibrin. Then the name vegetative endocarditis is not as yet justified.

**Course.**—If the process is superficial, only the base of the coating shows organization, and everything regresses except a scar-like circumscribed thickening, often hardly recognizable (see Amster, Felsenreich and v. Wiesner). Deeper injury leads to a chronic inflammatory granulation process in the valve tissue—chronic fibrous—or better, fibroplastic endocarditis—which frequently ends in thickening and cicatricial shriveling of the whole valve. This is frequent in articular rheumatism.

Chronic endocarditis may often assume an acute character from slight causes (recurrent endocarditis).

In the fibrous vegetations, newly formed vessels remain long after cessation of all inflammatory symptoms, and according to Koester, are

predisposing factors in new bacterial growth in which emboli are frequent (see p. 36).

Caution is necessary not to interpret every grayish red coating on a changed valve, as a newly implanted endocarditis. It may be only a simple thrombotic precipitate (see p. 24).

**Localization of the Vegetations.**—They favor certain locations. On the auriculo-ventricular valves, they choose the auricular side on the thickened, often uneven, edges, or at some distance from the free edge, not rarely they are shaped like delicate wreaths. On the semilunar valves, they are usually on the ventricular side on the margins of closure, but also

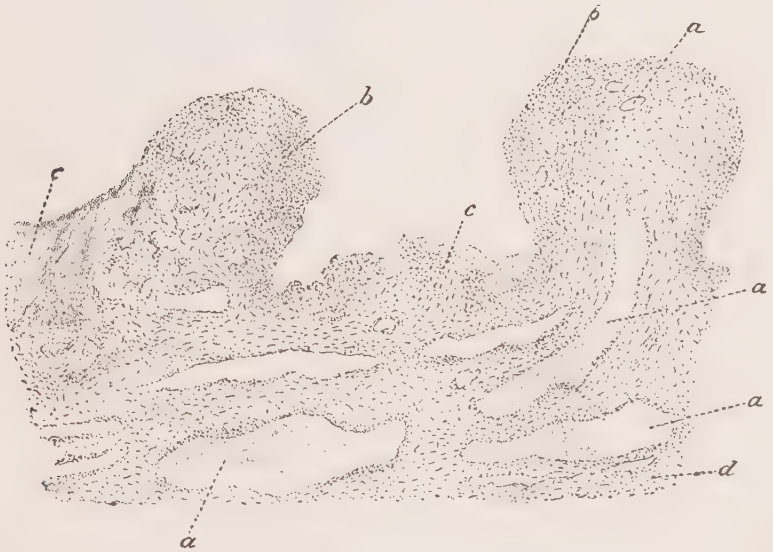



FIG. 7.—Subacute verrucose endocarditis of mitral valve after articular rheumatism; a, blood vessels; b, cellular granulation tissue; c, thrombotic masses; d, valve tissue with wide vessels; (low power).

above this point. Every region of the valve, the chordae tendinae and the whole endocardial lining may, however, become the seat of inflammation. The mitral and the aortic valves alone, or together, are the most frequent sites, the tricuspid valve is second choice. In embryonal life, the valves of the right heart, which at that time work harder, are affected more frequently, especially those of the pulmonary arteries.

The so-called noduli albini may be mistaken for vegetative endocarditis. They are found on the free rim of the tricuspids in the newborn, and are small connective tissue growths, remnants of the fetal gelatinous valve crest which disappears later. Frequently, in the newborn and even in later fetal months, there are found 3 to 6 minute, poppy seed-like, blood nodules or cysts on the auriculo-ventricular valves, (both surfaces), or

distributed over the whole surfaces. In the anterior mitral leaflet, they are only on the free edge; and they rarely occur in the aortic leaflets. They are dark red to black and project especially on the auricular side of the auriculo-ventricular valves. First they were thought to be valve hematomas (Luschka, Parrot), or hemorrhages into the soft loose valve tissue (Odinzow). Then they were taken for vessel ectasias (Berti, Koniger, Fahr, Hammes, Pepere), or even for angiomas (Nickols). On the other hand, Meinhardt (see also Haushalter and Thiry), demonstrated that these blood nodules which he calls saccular hematomas are formed by dilatation of preformed expansions on the valves, these expansions being supplied by a narrow channel-like opening lined with endothelium. Wegelin added further details, and recently Jonnson reconstructed them in wax. Wegelin, in a second work, differentiates (*a*) blood sacs or cysts, especially in children, rarely in adults (see also Bundschuh, Zurhelle, Wendel) starting from endothelial tubules and persisting from fetal life; (*b*) blood sacs developed from newly formed endothelial canaliculi in a manner analogous to valvular endocarditis, appearing in adults and which may be mistaken eventually for angiomas. The first form disappears during the first year of life; the blood breaks down, undergoes hyalin changes and organization, when the sac becomes smaller and is finally reduced to a pigment granule, or disappears entirely. Pigment can often be found in the valve tissues. The blood sacs of the second form also atrophy later. The aortic leaflets in children and adults may also show congenital thickenings separated from the free edges by a narrow margin but blending with the valve on the other side.

### Ulcerative Endocarditis

Septic, malignant, diphtheritic, deeply necrotic or acute destructive endocarditis.

This form, as mentioned above, is differentiated from vegetative endocarditis by the degree, and therefore often occurs simultaneously with the latter. The selection of special areas is not so striking, and the right heart is more frequently affected than in vegetative endocarditis. Microorganisms which quickly penetrate the depths of the valve, cause rapid destruction of tissue and separation of minute and larger pieces of the leaflets; in one case there is more necrosis (pure or with fibrin), in another more pus (purulent infiltration, liquefaction, purulent demarkation), and so on. While these ulcerative lesions are forming, precipitation of irregularly formed thrombotic masses takes place like warty coverings of globular or polypoid form often penetrated by masses of bacteria (figs. 8 and 11). They may soften and wash away, or organize; the destructive process may spread towards the surface and into the depth of the valve tissue as the

bacteria invade in every direction. Perforation readily occurs, or, a semilunar valve, *e.g.*, tears through. At other times, their attachments

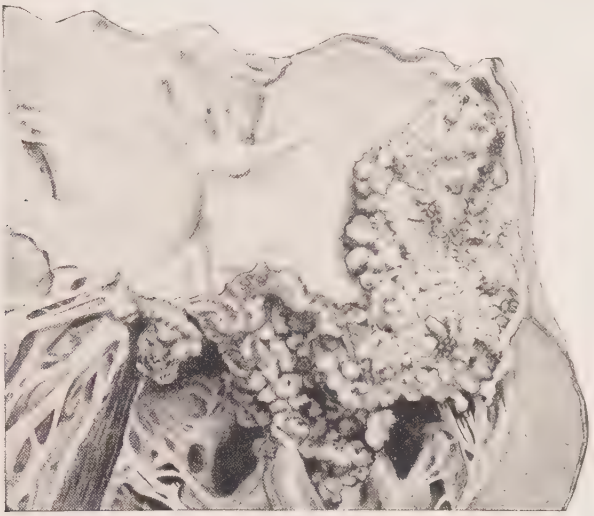


FIG. 8.—Insidious ulcerative endocarditis with marked thrombosis on the mitral valve extending to the endocardium of the auricle. Staphylococci in blood; fever and joint pains for 5 months; 18 year old student; 5/6 natural size.

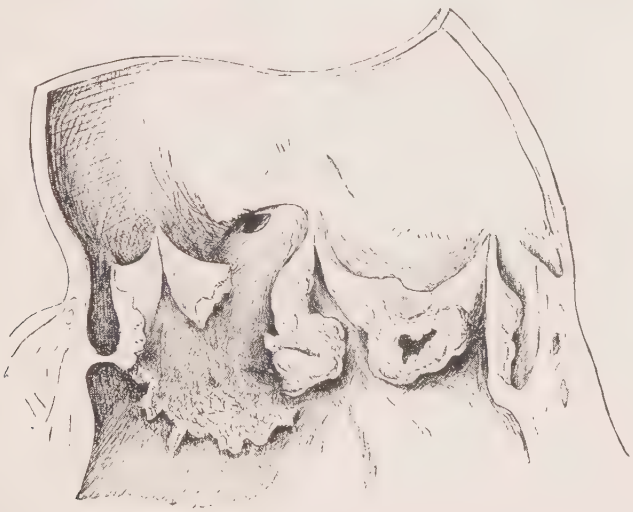


FIG. 9.—Ulcerative aortic endocarditis with acute valvular aneurysms, one of which (posterior or median leaflet) is perforated at the apex, while the aneurysmal right leaflet (r. coronary art. in the sinus of Valsalva) has torn through the middle; below, a large parietal endocarditic ulcer slightly covered with thrombi; left leaflet with entrance of the left coronary artery is divided by the cut.

are loosened or the process extends to the chordae tendineae and papillary muscles, (chordal and papillary endocarditis), and they are torn apart. The inflammation may extend by continuity to the surrounding tissue,

to the beginning of the aorta, rarely to the pulmonary artery, or to the mural endocardium, when the latter as well as the underlying myocardium may ulcerate (parietal ulcer); during this process thrombi may form again.

Isolated parietal endocarditis, as Deus (lit.) saw it in both ventricles, is very rare.

The development of ventricular or mural endocarditis is favored by floating valve tags which ofttimes have whip-like thrombi attached and whose influence may extend even to the arteries; parietal ulcers form

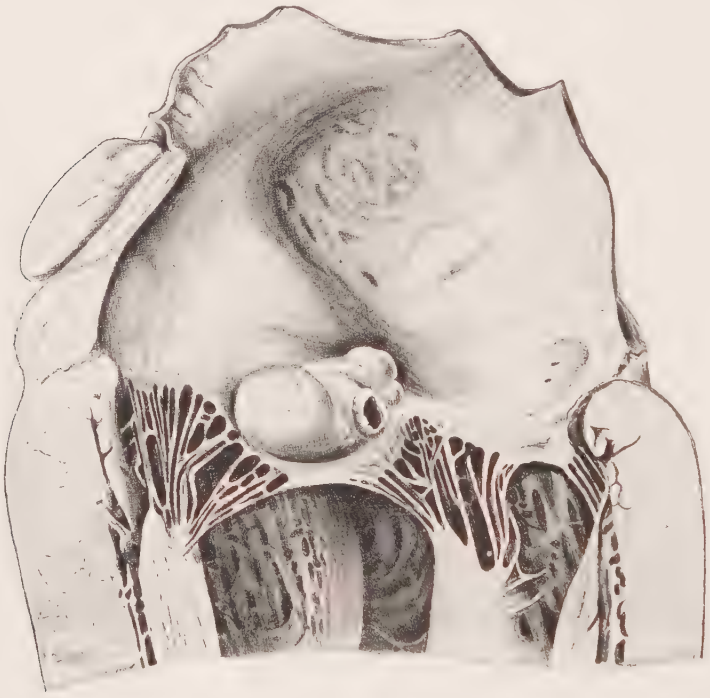


FIG. 10.—Chronic aneurysm on the aortic tip of the mitral valve perforated at a diverticulum-like projection. Above, the opened l. auricle; below, part of the l. ventricle below the divided mitral; man 30 years old; ⅓ natural size.

through implantation of bacteria and, if the thrombotic masses become calcified, they further traumatize the walls. These ulcers may penetrate so deeply that the blood pressure bulges the area outward like an aneurysm (ulcerative parietal aneurysm); there is especial danger when such a process involves the membranous septum which then bulges toward the right auricle or ventricle or toward the pulmonary arteries; thrombus formation is favored and perforation of the septum readily occurs.

Acute and chronic valvular aneurysms are very characteristic.

When a layer of the valvular endocardium is destroyed by progressive ulceration, a valvular aneurysm results. According to von Arx, throm-

botic masses and possible necrotic valvular fragments form a considerable part of the aneurysmal wall, being thrust into the sac by the blood pressure. The semilunar valves bulge toward the ventricle (fig. 9), the mitral valves bulge into the hollow of the funnel, *i.e.*, the auricle, when an ulcerative aortic endocarditis extends to the aortic leaflet of the mitral; in such cases the author saw sacs the size of beans. External thrombotic deposits aid in the thickening of the sac, but there is frequent perforation, with the torn opening growing slowly larger. In other cases the aneurysmal sac expands slowly until it reaches the size of a walnut, and then may contain thrombi or fluid blood. But perforation may also occur in this case. Very rarely a dissecting aneurysm (interparietal) develops (Pepere).

Primarily defective or misshapen valves are frequently the choice of an ulcerative endocarditis, for the friction of the margins of the aortic valves during diastole favors the lodgment of bacteria (see Kurz and Bauer, Kaboth, Beneke). In a 27 year old soldier, the author saw only two aortic leaflets with two symmetrically placed perforated aneurysms in the larger leaflet which corresponded to the normal right and posterior cusps; there was a short median line in the depth of the semilunars; the papillary muscles were absent, the chordae were inserted directly into the wall, the tricuspids were extremely thin, and the very thin pulmonary leaflets were fenestrated.

In reference to ulcerative aneurysms of the sinus of Valsalva, or at the beginning of the aorta from the progress of endocarditis of the leaflets of the aortic valve, or from possible implantation of bacteria in floating valvular attachments, see under arteries.

If an ulcerative endocarditis heals, as far as the valves are concerned, the same malformations result as discussed under chronic endocarditis.

Parietal endocarditis, seen not rarely in the left auricle and ventricle, leaves superficial or deeper tendonous scars; chordae, which were covered with masses of thrombi, may retain focal or diffuse thickenings, fibrous or smooth, or rough and calcified; torn chordae often have thick clubbed ends.

A quickly fatal ulcerative endocarditis which develops during a severe septic disease, and is rich in microorganisms may be called endocarditis mycotica maligna. The valves are discolored yellowish gray, and covered with a smeary coating. Thrombotic material is usually absent in any quantity. Defects develop quite frequently because the valves practically liquefy. Frequently, however, the general disease causes death before this can occur.

In the type called endocarditis lenta caused by the streptococcus viridans (see p. 36) there are often large numbers of phagocytic giant cells below the bacterial layer (see Orth). But the thrombotic coating may be very marked, but also very slight, as the author can verify.

Pneumococcic endocarditis often serves as an example of an infectious endocarditis with heavy globular deposits on an ulcerated base; it is

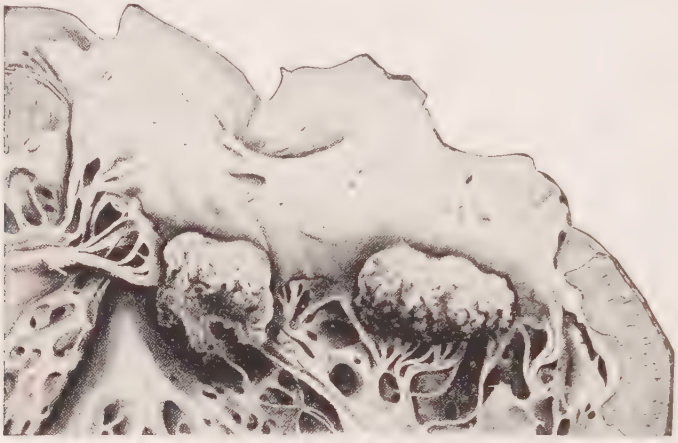


FIG. 11.—Globular endocarditis (gonorrheal); immense polypoid globular deposits on the mitral; 19 year old male; died 2½ weeks after infectious coitus (brothel); had also gonorrhea myelitis; 5/6 natural size.

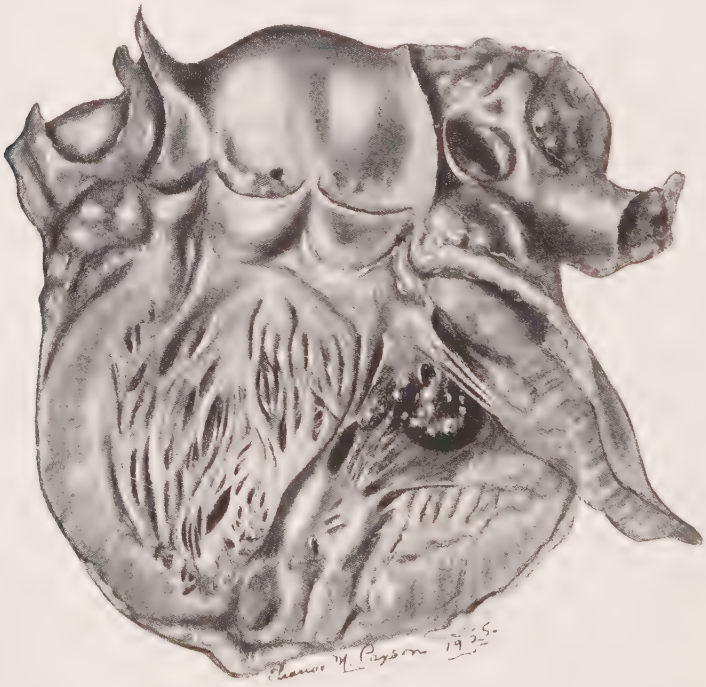


FIG. 12.—Vegetation of the mitral valve peeping out from underneath the portion of the left ventricle to the right. Present in a patient 35 years old. L. H. #67.

characterized by the unusual massiveness of the yellow green, broad-based globular thrombi on the ulcerated valves, but in the pneumococcic form the tricuspid is more frequently affected (Netter, Weichselbaum,

Kerschensteiner, Fiessinger-Rondowski). Emboli from these vegetations are often bland, but sometimes infectious. Pneumococci are often found in the vegetations, and in the organs generally, especially in the spleen which is considerably enlarged, (in one of our cases, 558 gms.); they are present also in pulmonary infarctions or abscesses, often in the involved meninges and even sometimes in the blood. We have seen this form of endocarditis in cases of pneumococcus bacteremia and pneumococcus sepsis in conjunction with pneumonia (reported by Wandel); the grayish green to yellow thrombi with smooth surfaces had a diameter up to 5 cm. on the tricuspid valves (see also Fulci). But pneumococcus endocarditis has also occurred with all the appearances of a common verruginous or ulcerative endocarditis (see Henke). And massive globular vegetations also occur in gonorrheal endocarditis, sometimes without much valvular destruction (fig. 11); again, in this form, a severe verruginous ulcerative process may occur, especially of the aortic and then the mitral valves (lit. by Schlagenhaufer), but milder forms are better known. Beitzke would like to differentiate polypoid endocarditis from verruginous and ulcerative, but according to our opinion, this is unnecessary.

### Etiology of Acute Endocarditis. Historical. Experimental

Endocarditis is either a secondary affection, *i.e.*, it arises from an infectious focus somewhere in the body, as in puerperal fever, surgical wound infections, pneumonia, osteomyelitis, urethral gonorrhea, etc.—from which bacteria enter the blood; or it is the primary localization of inflammatory factors which leave no demonstrable traces of disease where they enter the body. The former is by far the more common.

The two chief forms of acute endocarditis—verruginous and ulcerative—are only degrees of the same condition with essentially the same causes, infectious, or infectious-toxic factors in the blood stream. But in vegetative endocarditis, the necrosis involves only the superficial layers of the valve, perhaps only its endothelium, and formation of granulations takes place from the valve itself, while in ulcerative endocarditis with the rapid invasion of organisms, there is a severe necrotic and purulent destruction of the parts involved.

In the ulcerative septic form, the demonstration of the causative organisms is not difficult. This was first done by Heiberg and Eberth. Usually, they are cocci as in severe pyemia and septicemia (staphylococcus and streptococcus pyogenes).

In vegetative endocarditis, the mycotic nature of which was first pointed out by Koester and Klebs, and which is chiefly a concomitant of articular rheumatism although also of other infections such as measles, scarlet fever, pneumonia, typhoid, etc., the findings are less certain the

older the disease, because, as Bartel emphasized, the bacteria perish. Indeed, as in articular rheumatism, the actual cause of the affection may be unknown. Possibly it is a diplostreptococcus easily destroyed and unstainable, but active through its toxins (see lit. by de Vecchi, p. 64). Koniger attempted to explain amicrobic simple endocarditis through the possible action of bacterial toxins in infectious diseases—endocarditis toxica simplex, (see also Czirer and comp. p. 26).

Besides the staphylococcus and streptococcus pyogenes (the streptococcus viridans is frequently the cause of vegetative endocarditis, Schottmuller, Reye, and more rarely of the severer endocarditis lenta in which the leaflets become ulcerated), other organisms may be at fault, such as the diplococcus pneumoniae, (5 times in 43 cases of infectious endocarditis, Harbitz), the gonococcus, even when urethral gonorrhea is mild the distant metastasis may be marked, also B. influenza, coli, diphtheria, typhoid, actinomycosis, etc. have been found (lit. in appendix). Tubercle bacilli probably appear only as secondary arrivals in the vegetations. A verrucose or polypoid or diffuse caseating valvular tuberculosis is very rare (Fromberg). The parietal endocardium may also be invaded (lit. by Schultze). Michaelis and Blum claim to have caused tuberculous vegetations after injuries to the aortic leaflets and intravenous injections of tubercle bacilli. De Vecchi and Bernard, and Salomon could not obtain the same results; they saw only simple inflammatory reactions—necrosis, granulations and fibrin (see also Fulei).

The organized causes of endocarditis are consequently very many, and the activity of the same organism varies according to its virulence.

For this reason, it is easily seen why the cases do not always fit exactly within the boundaries of typical vegetative or ulcerative forms, but show quite frequent transition types; we called attention to an intermediate form sometimes caused by pneumococci; and there are rare forms in which pus, even pustule formation predominates (pustular endocarditis), while in other cases the discolored smeary bacterial coating appears as described on p. 33 (malignant endocarditis).

Koster claimed that, as a rule, endocarditis was due to embolism in the valvular vessels as demonstrated by him; recently, capillary emboli with modified and weakened organisms—pneumococci, as in Rosenow's animal experiments—are suspected, but other writers, especially Ruhle, are of the opinion that the organisms carried by the blood are precipitated on the valves and became fixed as oysters in oyster beds are fixed in spite of the force of the waves; a conception which later was verified by experimental investigations.

Experimental solution of the question of endocarditis was attempted by the traumatic method of O. Rosenbach, or by chemical injury of the

valves in animals combined with the injection of bacteria (staphylococcus or streptococcus pyogenes) into the blood. Endocarditis and metastatic pus foci developed (Orth, Wyssokowistch, Weichselbaum, and others).

Ribbert succeeded in producing endocarditis without previous gross damage, by the intravenous injection of an emulsion of staphylococci grown on potatoes. When coarser substances were present, bacterial attachment was favored, probably because of mechanical injury to the delicate endocardium, and although the localization showed marked differences from that seen in man, Ribbert was nevertheless able to trace the separate phases of the process, viz., the implantation of cocci on the endothelium, its destruction, the invasion of organisms into the valve tissue and the fate of the latter. Finally a large number of workers succeeded, but, of course, only in a small proportion of the experiments, in reproducing an endocarditis with the localization typical of that in man by simple injections of bacteria (see Lissauer, Rosenow, Saltykow, lit.).

It may therefore be assumed that endocarditis in man is analogous; bacterial masses are forced against the valves, therefore they select the margins, and then they either penetrate the tissues or remain superficial and cause thrombus formation and connective tissue overgrowth. To further illustrate this conception, it may be pointed out that endocarditis selects that part of the heart which works the hardest, *i.e.*, in extrauterine life, the left ventricle, in fetal life, the right ventricle, (Rokitansky, Rauchfuss, lit. by Thorel). But in addition, Vecchi demonstrated that toxins alone are able to initiate an endocarditis by causing primary necrobiotic processes, which are followed directly by active inflammation. Fibrinous thrombi may be added secondarily, and according to the predominant factor, ulcerative or vegetative forms develop (comp. negative results by Vanzetti and Fulci; positive results by Porrini). These experiments justify the thought of an infectious-toxic and perhaps also a purely toxic endocarditis—which latter would justify the conclusion that other chemical noxious substances may cause an endocarditis (Koniger) *e.g.*, in diabetes, nephritis, carcinoma, etc. For the present, however, it is impossible to pronounce judgment (comp. Panichi and Guelfi, and Panichi and Varni who report endocardial changes, thrombi, hemorrhages, following infusions and suspensions of carcinoma material, while Fulci, lit., and Panichi emphasize that this does indeed cause lesions, but not true endocarditis).

**Translator's Remarks.**—The form that has come to be known chiefly by clinicians as "subacute bacterial endocarditis" is anatomically a variety of verrucose endocarditis, but certain views merit attention. Libman would call it "subacute streptococcic

endocarditis" since in the great majority, anhemolytic streptococci are found when organisms are present at all; in a few cases B. influenzae are found and in a very few cases, other organisms. The duration of the disease is from a few weeks to two years, death resulting from exhaustion, anemia, sepsis, cardiac decompensation, uremia, etc. A characteristic symptom is the appearance of the so-called Osler's nodes—painful swellings to the size of a pea or larger on the fingers, toes, hypothenar and thenar eminences. At autopsy, the vegetations are coarse and found on the mitral valve, or extending to the mural endocardium, more rarely in other situations. During a septicemic stage, they consist in large part of bacteria; during a bacteria-free stage, healing may occur but usually so much damage has been done that the result is also fatal. The kidneys show various stages of chronic glomerulo-nephritis, but a more characteristic lesion is the discovery of partial, less frequently total infarction of isolated glomeruli. The other changes are secondary to anemia, cardiac decompensation, etc. See Libman Med. Clin. N. A., July, 1918, Practical Lectures pub. by Hoeber, N. Y., 1923–24, pp. 246–274. Clawson, B. J., Arch. Int. Med., 1924, 33, 157, Clawson, B. J. and Bell, E. T., Arch. Int. Med., 1926, 37, 66. For the kidney see Baehr, G. L., Exp. Med., 1912, 15, 330; Am. J. M. Sc., 1912, 144, 327; Arch. Int. Med., 1921, 27, 262.

### Chronic Fibrous Endocarditis (Better, Fibroplastic)

This results from an acute, principally rheumatic, endocarditis, and is a chronic inflammation with connective tissue production and subsequent contraction, (endocarditis retrahens); when it finally disappears, scar tissue remains. It is essentially a consequence of acute endocarditis, and leads to valvular thickenings, adhesions, shrinkings, and to mural scar-like thickenings, or superficial or deeper tendinous scars (parietal endocardial fibrosis).

There is always a new growth of vessels at the valve base as demonstrated by Ribbert by injections.

It is rare to have a diffuse chronic fibrous parietal endocarditis with cicatricial change of the inner surface, especially of the left ventricle, without valve changes such as dilatation and thrombosis (Baumler). But a thickening of functional origin, the so-called functional elastic parietal endocardial fibrosis, as a result of increase of blood pressure in contracted kidney, etc., is quite frequent; (see Hertel, see also p. 46 and thrombogenous parietal fibrosis from capillary thrombi). A superficial verrucose endocarditis may soon heal without trace (see p. 28), but if the

inflammation extended into the deeper layers and involved larger areas, connective tissue proliferation is likely to result, because the necrotic bits and possible thrombotic deposits act as chronic irritants and stimulate the proliferative process. If an ulcerative endocarditis heals, it is accomplished only by an active and continued connective tissue proliferation sufficient to cover the extent of the necrotic, ulcerative, and thrombotic changes. This must lead to thickening, shrinking, adhesions, and fibrous organization of thrombotic deposits which in a word means a deformity of the valve, perhaps only of a single leaflet, but often to an extent that the valve is hardly recognizable. It is especially in these cases that the parts turn yellow and become stony hard from petrification, (p. 23), or even true ossification.

It may also happen that two leaflets fuse into one, which must not be mistaken for a congenital defect, especially if the latter chances to show inflammatory lesions (see pp. 33 and 97).

If one or more new acute infectious processes occur during the course of chronic endocarditis, it is spoken of as recurrent endocarditis. Bacterial implantation is favored by this place of lowered resistance and also perhaps by the newly formed vascularization, (superficial in the one case, and intravascular in the other).

Chronic valvular endocarditis is met most frequently in the mitral and aortic valves, more rarely in the tricuspid and pulmonary, and sometimes in all the valves.

The changes consist of adhesions of the leaflets, most frequently of the tricuspids, or retraction and shortening. The mitral becomes a short, thick-walled, stiff funnel, with a slit or sickle-shaped opening; the ostium is stenosed and there is insufficiency. In the semilunar valves, retraction is most frequent. The leaflets of the aortic valves become rolled inward, thickened, stiffened, insufficient, or the ostium becomes stenosed, but they also may adhere to each other, especially at the angles, or to the wall of the aorta. A cylindrical, club-like or spindle-shaped thickening or adhesion of the chordae tendineae is very frequent, but an inflammatory right or left conus stenosis is rare (lit. by Dilg).

To understand the final diffuse cicatricial change, especially of the mitral valve in rheumatic endocarditis, it must be pointed out that a large part of this valve fibrosis is secondary, that it is due in part to the function of the changed valve, and to the increased blood pressure caused by its insufficiency (Adami, see also Beneke). Secondary parietal endocardial fibrosis and fibrosis of the papillary muscles may also be found under these conditions (see p. 46).

Very often there appear on the fibrous valvular thickenings whether due to endocarditis or secondary, regressive changes (discussed, p. 22)

resembling sclerosis and atheroma of the arteries; even ossification may occur (see Rohmer).

As mentioned above, thrombotic masses may be deposited so that recurrent endocarditis is simulated, or, on the other hand, it is easy to overlook a primary simple degenerative change of valve tissue with its concomitant and subsequent consequences. The differential diagnostic difficulties as mentioned on p. 25, must again be pointed out, *i.e.*, the distinction between an older primary degenerative change of the endo-

FIG. 13.—Stenosis and mitral insufficiency due to endocarditis. Mitral leaflets thickened web-foot-like adhesions of the thickened chordae tendineae; fibrous transformation of the tips of the papillary muscles; contraction of the aortic leaflets due to fibrous endocarditis; insufficient aortic valve; dilatation of the left ventricle; dilatation of the tip; flattening of the trabeculae; upward movement of papillary muscles; the plump left auricle is filled with thrombi.

cardium of the valves and a healed endocarditis with connective tissue thickening. The chief difficulty is due to the reactive proliferating processes following degenerative changes, especially if thrombi are deposited, for sclerosis and nodular thickenings are produced to degrees sufficient to cause functional disturbances. On the other hand, regressive changes often occur in the connective tissue of a valve which was thickened by a previous endocarditis but, on the whole, the less degenerative change in the connective tissue, the more its development is suggestive of chronic endocarditis. (Histological criteria of inflammatory thickening of valves

by Felsenreich and v. Wiesner, lit.; see also Czirer; also Felsenreich and v. Wiesner in reference to peculiar histological degeneration pictures—skein and loop formation on the valves in chronic endocarditis (for differentiation on the basis of localization see p. 25.) [See also Clawson, Bell, Hartzell, Am. J. Path. 1926, 2, 193.—*Translator.*]

Calcification on the fibrous ring (annulus fibrosus) surrounding the aortic and the mitral ostium is independent of endocarditis but is seldom present in large amounts; in endocarditis however, it may become a chalk ring as thick as a finger, reaching to the musculature as a nodular, continuous or beaded deposit. Bone may also be deposited (heart bones). The author saw such a case in which a broad prolongation penetrated the musculature for several centimeters and bulged through the posterior wall of the ventricle under the epicardium.

For amyloid endocarditis, see Goldzieher; also pp. 23 and 55.

### Consequences of Endocarditis

The most important consequences of endocarditis are: 1. emboli; 2. valvular lesions.

### Emboli

They may be (*a*) infectious, washed off from the valves in ulcerative endocarditis, reaching the lungs from the valves of the right heart, and the greater circulation from the left valves and thus be carried to different organs—heart muscle, pericardium, spleen, kidneys, eye, perhaps with occlusion of the central retinal artery (lit. Kober); they may enter the arteries of the legs, skin, etc. and be followed by metastatic abscesses, (embolic septic pyemia), in fact, any organ may be involved. Frequently, the emboli are small (capillary) and consist only of organisms which actually flood the organs. They are easily demonstrated in the glomeruli of the kidneys. In ulcerative endocarditis, innumerable punctate hemorrhages appear in the skin (hemorrhagic exanthema), the internal organs, serous membranes, kidneys, brain, retina. They are considered due partly to toxic influences. Among others, Simmonds describes brain hemorrhages due to embolic aneurysms.

(*b*) Non-infectious or bland emboli are usually released in vegetative endocarditis, by the detachment of bacteria-free thrombi; these produce simple mechanical vessel occlusion (ischemic necrosis, infarction), but it must be remembered that non-infectious infarcts may occur from even severe ulcerative endocarditis (Lenhartz).

Large emboli are capable of occluding large vessels, particularly when they consist of detached tags of ulcerated endocardium.

Detached pieces of calcified thrombi cause peculiar lesions when they enter vessels as emboli (see embolic aneurysm).

### Valve Lesions (Heart Failure)

Organic valve lesions produce functional disturbances (stenosis and insufficiency) of the valvular mechanism and are due to both endocarditis (infectious or non-infectious), acute or chronic, and purely degenerative processes (p. 22). But in addition to these, and congenital valve lesions, we must call attention to the tearing of leaflets and muscles from intensive physical exertion or trauma, such as blows, falls, pressure, etc., (lit. by Stern, Rimbaud, Kulbs, Steinitz, Schwartz, Beckhaus, Berblinger). Functional disturbances in rare cases are due to tumors.

(*a*) Stenosis is the result of such chronic conditions as fusion of the margins, hardening from calcareous infiltration of thrombi, and shortening of valves; it rarely develops in the acute lesions, but abundant excrescences and thrombi may partly obstruct the opening.

(*b*) Insufficiency, valvular insufficiency, incontinence, inability to close, may be acute or chronic: acute, from tearing of chordae tendinæ and from perforation of leaflets; chronic, as a result of scar retraction,, shortening, rolling inward, fibrous induration, (the valve becomes stiff), adhesions of the segments with the ventricular or vascular parieties; deposits and attachments, acute or chronic, may also prevent closure of a valve.

(*c*) Stenosis and insufficiency are often combined, especially in chronic valvular lesions, since the same factors may prevent both opening and closure.

In so-called relative valvular insufficiency, there is no anatomical change in the valve itself, (or, at least, not necessarily so); its end results are similar to those of organic insufficiency. Its direct cause is a widening of the valve ostium; the valves retain their original size but are too short to close the enlarged lumen. It is most frequent at the tricuspid, which normally, hardly permits admittance of three fingers; next in frequency, it occurs at the aortic valve.

Valvular insufficiency (muscular insufficiency) chiefly of the venous openings, more rarely the aortic, is due to faulty ventricular or papillary muscular contraction as from fatty degeneration, scar formation in the musculature, or insufficient nutrition as in chlorosis and anemia.

These are the cases in which perceptible sounds during life suggest the probability of valve changes, which, however, are not found at autopsy. The reverse may also happen, the presence of severe valvular changes, *e.g.*, extensive vegetations, or typical old changes, (functionally healed endocarditis? Amsler) may not give the slightest auscultatory symptoms.

The most active factor in closing the leaflets of the auriculo-ventricular valve is the musculature itself, because the leaflets form a narrow funnel with lateral foldings and do not function as a sail, but as a tube valve (Koster). According to Hesse and Krehl, the valve leaflets bend and bulge into the auricle during systole in such a way as to close it above, and their lower edges are forced flat together. According to Magnus-Alsleben, the large anterior mitral leaflet acts in conjunction with the wall of the septum almost as a discharging tube or communication between the ventricle and the aorta. According to Nussbaum, the closing of the mitral valve (formalin fixation in systole) is caused by forward bulging between the chordae tendineae. The so-called senile thickening consists of a fixation of this systolic bulge.

Relative insufficiency of the aortic valves occurs from arteriosclerotic weakening and distension (aneurysm) of the aorta and also from idiopathic cardiac hypertrophy.

Both relative and muscular insufficiency regress if the musculature is able to recover.

## Anatomy of the Valvular Lesions

### mitral lesions

(*a*) **Mitral Stenosis (Fig. 13).**—The left atrio-ventricular ostium of adults usually admits 2 fingers; its circumference is 10 cm.; when it is narrowed, the passage of blood is hindered from the left auricle into the left ventricle (diastolic sound of varying intensity); the blood is dammed back into the auricle which it distends, and stimulates to compensatory hypertrophy. The distension may be enormous; the left auricle reaches around behind the right auricle forcing the right lung outward; its cross section may measure 20 cm., and the sagittal section, 14 cm. In the case of G. Muller, it contained 2.5 and in Minkowski's case, 3 litres of blood. The left recurrent nerve may be compressed and paralyzed (Alexander, Stoerk, Schuberth and others). Its relation to the esophagus is discussed under esophagus.

This damming back extends from the left auricle through the valveless pulmonary veins, to the pulmonary capillaries which are convoluted from overfilling; in cases of longer duration, red induration of the lung takes place, the congestion extending to the pulmonary arteries and to the right ventricle. The latter dilates, and attempts to compensate lead to its hypertrophy. Its inability to empty completely is transmitted to the right auricle possibly causing relative insufficiency of the greatly stretched tricuspid; then during ventricular systole, some blood flows back into the auricle. This damming back can be felt from the right ventricle to the most distant veins of the body (cyanosis of the ends of the fingers).

In slight degrees of stenosis the overfilling of the left auricle causes no lesions as long as the right ventricle overcomes the resistance by compensatory hypertrophy. For this reason, mitral stenosis may be endured for many years without great disturbances. But in severe stenosis or failure of compensation of the right ventricle, the left ventricle receives less blood, its work is diminished, the muscle atrophies, and the ventricle, as a whole, becomes smaller. (It does not atrophy, according to Wideroe; for this

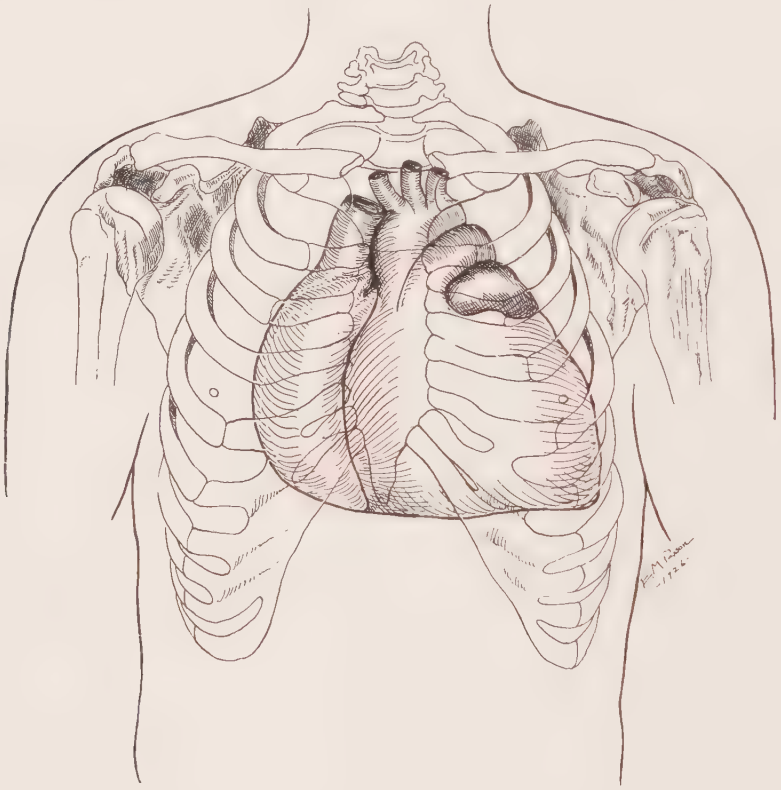


FIG. 14.—Diagram showing the relative size of the heart and thorax in acute dilatation. This happens to be in a patient with mitral stenosis but may well illustrate the dilatation which occurs in other valvular defects. L. H. #119.

disputed point, see Lenhartz, Baumbach, Oestreich, and lit. by Thorel.) [For the surgical treatment of mitral stenosis see Cutler, E. C.; Levine, S. A.; Beck, C. S.; Arch. Surg. 9, 689, 1924.—*Translator.*]

(*b*) **Insufficiency of the Mitral Valve.**— During the systolic contraction of the left ventricle, blood flows backward into the left auricle through the insufficient valve (blowing systolic sounds). Because the latter receives more blood than usual, it dilates, and the effect is finally transmitted to the right ventricle which also dilates and hypertrophies as in stenosis.

But the left ventricle reacts quite differently. During each diastole, it receives the blood dammed back in the overfilled auricle and is thus distended and hypertrophic. (comp. Shapert; hydrostatic test:—open left ventricle at its apex, carry in rubber tube to fill with water. compress the aorta, examine mitral leaflets from the opened auricle).

Thus all parts of the heart are dilated and hypertrophic.

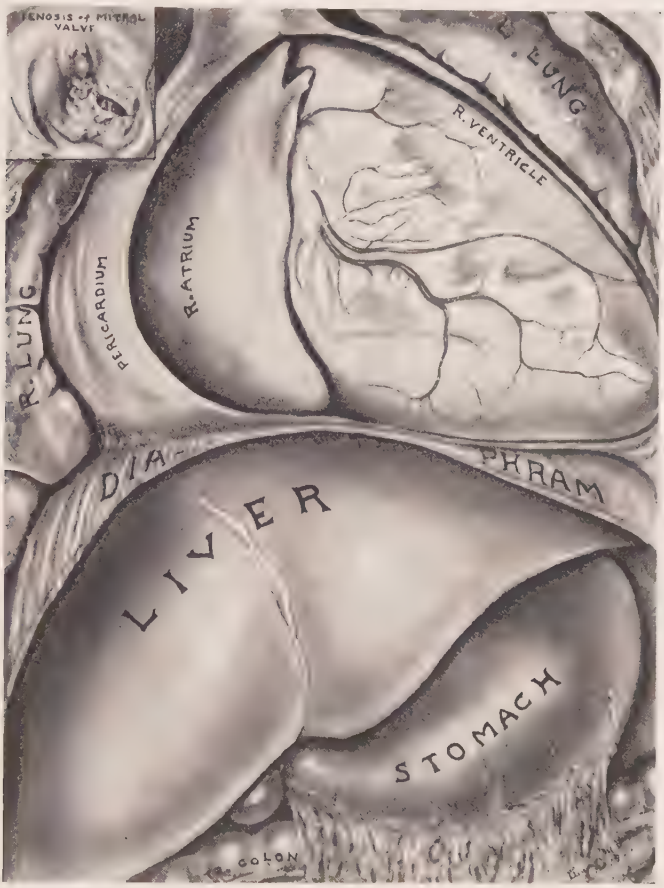



FIG. 15.—Acute dilatation of the heart with mitral stenosis showing the size of the heart and its relationship at the time of autopsy. L. H. #119. Man, 24 years old.

(*c*) **Stenosis and insufficiency** are very frequently coincident in the mitral valve which usually shows chronic changes.

### LESIONS OF THE AORTIC VALVE

Normal width of the opening is 7 cm.

(*a*) **Stenosis,** (rarely pure), increases the work of the left ventricle which must force the blood through a narrow ostium (loud systolic murmur). The blood is thus dammed back in front of the valve. This causes

hypertrophy of the left ventricle only; if its musculature is powerful, it assumes an ovoid shape and bulges into the right ventricle which is like a flat appendix to the heart. When the left ventricle ultimately dilates, there is prompt damming back of blood into the left auricle and from thence into the lesser circulation, while the greater circulation receives less arterial blood than normally (anemia of the brain).

By subvalvular stenosis of the aorta is understood the formation of a fibrous stenosing ring about 2 cm. below the valve, attributed to a fetal endocardial thickening, (Jagic and Schlagenhaufer, lit.).

(*b*) **Insufficiency** (**Fig. 13**).—During diastole the blood flows back into the left ventricle, through the insufficient valve of the aorta (diastolic blowing sound); the ventricle dilates and hypertrophies; similarly, the aorta, which of course contains a larger volume of blood during systole, also dilates. In this way, very marked cardiac enlargement is brought about (cor bovinum).

As a result of the increased pressure during systole in stenosis, or from the impact of the regurgitating blood stream in insufficiency, calloused, crescent-shaped ridges or folds (regurgitation scars), or "pockets" develop in the endocardium of the left conus arteriosus (Zahn), which occasionally expand like semilunar valves (Schminke) but with no suggestion whatever of functional adaptation or purpose (see Wilke, Steinitz, Rosenbusch, lit. Dewitzky). These structures were considered by Sotti as partly congenital in origin. Syphilitic aortitis is often accompanied by aortic insufficiency from either bulging, shortened, thickened, stiff valves or by reason of relative insufficiency from dilatation of the aorta. Adlmuller (lit.) found that 74% of cases of aortic insufficiency were due to lues. Further details under aortic syphilis.

### LESIONS OF THE TRICUSPID VALVE

The normal width of the ostium is 12 cm.

Organic changes, stenosis or insufficiency, are very rare compared to relative insufficiency (see p. 42). Stenosis is rarely very marked (see Brieger, lit.).

### LESIONS OF THE PULMONARY VALVES

The normal diameter of the ostium is 8 cm.

Stenosis and insufficiency are mostly congenital; the former is far more frequent.

### Frequency of the Different Valve Lesions

Mitral lesions, chiefly insufficiency, constitute almost ⅔ of all valvular lesions; next in frequency are those of the aortic valves, especially insufficiency—then combined lesions of both valves, and eventually of the others

also. But other heart lesions are much less in number. Comparatively, the most frequent of these is relative insufficiency of the tricuspid consequent to mitral lesions. Mitral lesions are perhaps more frequent in women; lesions of the valves of the aorta (which are more chronic), are more frequent in men.

### Congenital Heart Lesions

(Chief symptom: congenital cyanosis, see p. 90 and following.)

They are rather rare; the most frequent are stenosis or atresia of the pulmonary artery, and lesions of position of the septa, and of the large vessels.

### Relation of Cardiac Valvular Lesions to Pulmonary Tuberculosis

Congenital stenosis of the pulmonary arteries is a predisposing factor in pulmonary tuberculosis. Left heart lesions combined with pulmonary venous congestion, offer a relative pulmonary immunity to tuberculosis (other details, under congestion of lung).

### Consequences of Valvular Lesions

(*a*) Abnormal distribution of blood, *i.e.*, damming backward (excess of blood) in front of (in regard to the direction of the blood stream) the diseased valve, occurs in stenosis because all of the blood cannot pass through the narrowed opening,—while an incompetent valve allows regurgitation.

This stasis extends backward until a valve interferes, *e.g.*, from the left auricle through the lungs to the right ventricle. Behind the diseased valve there is anemia which continues onward into the arterial system, while hyperemia is present in the venous system.

The results of lesions in the right and left heart differ in that the anemia in the former extends through the pulmonary artery forward into the aortic system, while in the latter, it does not affect the lesser circulation. In the right, damming back involves only the territory of the cavae, in the left, it also includes the lungs.

(*b*) **Changes in the Diameter of the Cardiac Chambers.**—Damming back of the blood stream causes dilatation in front of the valvular lesion, while the part behind the valve is not sufficiently filled because of the narrowed orifice (eventual diminution in size of the cavity).

As the cardiac energy diminishes, parietal thrombi are occasionally deposited in the dilated chambers (see under myocardium).

(*c*) Changes in the thickness of the walls consist of (aa) thinning from distension through excessive filling, or atrophy from constant decreased filling (this is disputed, see under left ventricle in mitral stenosis); (bb)

thickening, compensatory hypertrophy occur when there is greater difficulty in emptying the overfilled cavities but there must be a musculature capable of compensation; as soon as this is accomplished, abnormal distribution of blood ceases.

2. Consequences to the whole organism appear as soon as compensatory disturbances occur.

The most spectacular change is congestion with cyanosis. This involves:

(*a*) The lesser circulation with red induration of the lungs, "herzfehler" cells in the sputum, hemorrhagic infarction, bronchial catarrh, pulmonary edema, etc. Cardiac cases frequently die from pulmonary edema.

(*b*) The greater circulation in which there is general cyanosis, cyanotic atrophy of the liver, cyanotic induration and later atrophy of the spleen and kidneys, (albumen-containing "cardio-renal" urine), hemorrhagic endometritis, finally hydrops of cavities, and edema, especially of the legs.

(*c*) The portal system (ascites, gastric and intestinal catarrh).

In congenital right heart lesions there occur the highest degrees of cyanosis.

Embolic processes may appear in the peripheral parts and in the internal organs such as lungs, spleen, kidneys, brain, etc., (see p. 41).

[For acute endocarditis following war wounds, see Karsner, H. T., Arch. Int. Med. 22, 296, 1918.—*Translator.*]

## MYOCARDIUM

**Anatomy.**—The protoplasm of the closely connected syncytium forming the heart muscle fibres is partly differentiated into cross striated fibrillae, but the greater part lies chiefly in the fibrillary axis and remains as undifferentiated sarcoplasm. Within this, lies the nucleus; its size and chromatin content vary, and its flat cylindrical, wavy form changes with systole and diastole (lit. in appendix).

Prolongations radiating from the sarcoplasm between the fibrillary bundles constitute the longitudinal striations of the muscle fibre. According to Hoche, M. Heidenhain, and others, there is also an exceedingly delicate sarcolemma most difficult to stain; this is disputed by v. Ebner, while Schaffer speaks of a fine membranous network passing between the fibres. The muscle fibres show straight or step-like graded lines running transversely. Formerly the opinion prevailed that these were "cement lines" of muscle cells (see also Ehrenfried, Albrecht), then artefacts or post mortem atrophy contractions were spoken of (v. Ebner, Stamer, Aschoff, Sapegno), but Heidenhain viewed them as insertions to serve lateral growth. According to Dietrich, (lit.), the cross striations are a

sort of thickening, a bunching together of fibrillae so that they can exert their power by pulling; this opinion is shared by Ogata who found the striations in the fibres of the bundle of His also. v. Ebner, abandoning his older theory, now considers the "shiny lines" special differentiated fibrilla sections corresponding in the relaxed fibre to an especially marked insertion disc, and in the contracting fibre to an exceptionally thick contraction strip which develop in the course of extrauterine life as an important functional adaptation for the regulated contraction of the muscle fibre network. They are absent in the heart of the newborn. Compared to other cross striated muscle, heart muscle fibres have the characteristic short oblique or diagonal anastomoses of the fibres, the central nucleus, the finer cross striation, and last, but not least, the cross lines (cement lines).

For more details as to difference in the muscle fibres of the auricles (less marked striation, more sarcoplasm, larger nuclei, less pigment, and greater abundance of connective tissue) see Aschoff-Tawara, v. Palczewska, etc.

See Berblinger in reference to glycogen of the heart and its distribution, and Rainer, for the lymphatic system of the heart.

## Parenchymatous (Muscular) Diseases of the Heart

### Atrophy of the Heart Muscle

There may be differentiated: simple atrophy, a regressive nutritional disturbance in which the muscle fibres become smaller so that the size of the heart as a whole is diminished; a typical example is "brown atrophy" in which the smaller fibres are markedly pigmented and the muscle appears brown macroscopically.

Both changes are found in inanition, in death by starvation, or in hunger atrophy in both its narrow and broad meaning; the food is either not supplied, or however abundant, is not able to replace the metabolic losses. The nucleus may also be smaller, (comp. Heitz), as in various cachexias such as in neoplasms, especially carcinoma, phthisis, etc. Brown atrophy is found especially in the aged and is a symptom of senility. In an 18 year old girl with extreme stenosing fistulous intestinal tuberculosis, the author saw a heart weighing only 100 gms.

But according to Wideroe, the other tissues, musculature and organs, are affected by senile atrophy to a more marked degree than the heart.

The pigment, microscopically yellowish brown, lies in the form of granules in the sarcoplasm at the poles of the nuclei. Spindle shaped figures around the nuclei are formed at the poles from deposits of pointed pigment masses (fig. 16). This pigment does not give an iron reaction.

Its origin, like that of normal muscle pigment, is possibly from nuclei products; it is usually classed with the fat-containing so-called waste pigments (Lubarsch). According to Ribbert, it is the slag of the combustion processes of the protoplasm, but Schmidtmann thinks it is a sulphur-containing melanin derived from protein, and the fat in the granules (fat stain) is only an admixture; therefore it is not lipofuscin, but melanin, similar to the pigment of brown atrophy of the liver; (see under liver for other opinions).

For iron-containing pigment in muscle fibres and interstitial tissue, see J. D. Freiswerk—also for hemochromatosis (comp. pigment cirrhosis of the liver).

Slight microscopic degrees of brown pigmentation are found even in children, but there is no atrophy.

FIG. 16.

FIG. 17.

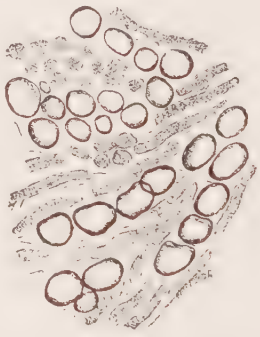


FIG. 18.

FIG. 16.—Brown atrophy of the heart; pigment accumulation at the nuclear poles; isolated pigment granules scattered in the fibers; (med. magn.).

FIG. 17.—Fatty degeneration of the heart (med. magn.).

FIG. 18.—Fat infiltration between fibers of heart muscle which have been forced apart and became atrophic; fresh, unstained (low power).

In the excessive degrees of pigment atrophy the granules may be scattered within the muscle fibres, or between them, in which case they probably originate from destroyed fibres. The connections of the muscle fibres appear loose and the "cement lines" become more distinct.

Macroscopically, the heart of brown atrophy is small, often markedly so, (⅔ to ½ of normal). The apices of the papillary muscles show fibrous change; Kirch describes a "slipping down" of papillary muscles, especially the left, and shortening, narrowing, and pointing of the intrapapillary spaces. In marked degrees of atrophy the coronary arteries are usually contorted because they are too long for the small heart. This is to be distinguished from the lengthening and contortion of the coronary arteries in arterio-sclerosis (aneuryma cirsoides).

The epicardium and endocardium are not infrequently wrinkled and thickened. The color is dark brown or chestnut, the consistency normal,

or, more frequently, increased and tough. When fatty degeneration is added, the heart is soft and fawn colored.

If the heart was formerly hypertrophic, it may still be of considerable size, notwithstanding brown atrophy. The senile heart hypertrophic from emphysema or arterio-sclerosis, or even without these, (the large heart of a sturdy old man) often shows slight brown atrophy in its hypertrophic musculature (see also *Ribbert*, and p. 72).

### Parenchymatous Degeneration, Cloudy Swelling and So-called Fatty Degeneration

Microscopically, cloudy swelling produces a cloudy gray appearance of the muscle substance, due to innumerable minute protein granules which have the appearance of dust, while the cross striations of the thickened fibres completely disappear.

Fig. 19.—Papillary muscle with fatty degeneration.

This change can be well observed only in fresh, unstained preparations, and by addition of 1% acetic acid, and potassium or sodium hydroxide, the clear granules swell and dissolve and so disappear, (protein-reaction), while the nuclei stand out more sharply.

This condition accompanies high fever, especially in the infectious diseases (sepsis, diphtheria, scarlet, typhoid, etc.), and various poisonings, grave anemias, etc. Macroscopically, the heart muscle has a lighter, spotted, grayish brown, opaque (cloudy), appearance (normally shiny), especially the inner layers, and is relaxed, softer, somewhat friable and easily torn.

Care must be taken not to confuse this with post mortem clouding without swelling, but with fragility of the heart muscle. This latter is a coagulation process. If decomposition is rapid, the heart muscle becomes quite friable, is brownish yellow, or, by imbibing liquids, dirty brownish red, is filled with decomposition bubbles and the heart cavities are markedly distended by gas formation in the blood. The valves and the beginning of the aorta are discolored, (sanguinous imbibition), (see p. 25).

In the so-called fatty degeneration (fig. 17) which may follow cloudy swelling or appear independently, highly refractile granules and droplets of fat of varying sizes appear in the muscle fibres, at first isolated, later more abundantly, finally causing complete disappearance of cross striation and nuclei. The degree of fatty degeneration varies considerably (see p. 53).

The fat granules are first arranged in parallel rows in both the longitudinal and transverse directions (mild degree), but as the disease becomes more severe, the latter arrangement is more and more obscured, although

the longitudinal arrangement may remain. The so-called cement lines are very plain. In the most advanced degrees, the fat droplets are large, reaching the size of an erythrocyte, or a leucocyte, and every geometric arrangement disappears, but the nuclei are still demonstrable by the addition of acetic acid.

**Reactions to Fat.**—The shining droplets are insoluble in acid and alkalies, but a 0.5% potassium hydroxide solution dissolves the contractile substance and causes the fat droplets to stand out better by contrast.

Fat dissolves in ether and alcohol, stains brown to black with a 2% aqueous solution of osmic acid, red with alcoholic solutions of sudan. Sudan stains neutral fat and fatty acids red, the latter with a somewhat brownish tinge. Nile-blue sulphate stains neutral fat purple, fatty acids indigo blue, lipoids reddish blue to violet (see Stheeman). In fat-protein combinations in which chemical analyses can demonstrate fat, the microchemical staining reactions fail (see also p. 53).

Macroscopically, the heart muscle first appears spotted, then diffusely yellow, although some areas, but without definite localization, are changed more intensively. According to Goebel, the most markedly degenerated parts of the musculature are located chiefly under the epi- and endocardium close to the interstitial connective and fatty tissues. Frequently, the spots show a delicate tracery, the so-called "fat etching," which is especially visible on the trabeculae and papillary muscles in the form of zig-zag lines (lightning figures), arranged transversely to the direction of the fibres.

According to Ribbert, the areas of fatty degeneration correspond to the venous circulatory areas where impaired nutrition or oxygenation prevented complete oxidation of fat in the cells (for contrary opinion, see Borcher).

In high degrees of fatty degeneration, the muscle becomes flabby, fragile, cloudy gray to pale yellow, all depending on the degree of associated anemia. Often the cavities are distended and the walls thinned. If there is brown atrophy as well, a fawn color results. In the child's heart, the change in consistency is usually not so marked.

Fatty degeneration is exceedingly frequent in many different conditions. Quantitative and qualitative blood changes with diminution of the oxygen supply seem to especially favor its development.

For this reason we see it most marked in pernicious anemia, in faulty blood formation and sometimes also in leukemia.

We see fatty degeneration in infectious diseases, especially diphtheria, sepsis, scarlet fever; in bacterial toxemias, in high fever of long duration, in poisoning by phosphorus, arsenic, chloroform, (but only slight, according to Bock), iodoform, ether, alcohol (in the latter it may cause sudden

death especially among dram drinkers, Richter); poisonous fungi (M. B. Schmidt, Herzog); after severe loss of blood; from local disturbances of the nutrition in coronary artery disease, (narrowing, occlusion); following increasing pressure of pericardial exudates, etc. We also see it in more than one-half of all cases as the finale of hypertrophy in valvular lesions, (see also p. 75); in chronic renal affections, emphysema, kyphoscoliosis, etc. Fatty degeneration seems to be a proof of the inability of the heart muscle to continue its compensatory work (secondary fatty degeneration). In valvular lesions a single papillary muscle, usually on the left side, is especially diseased.

In the newborn, fatty degeneration occurs in Winkel's disease which chooses by preference sturdy infants who perish in the first few days with the symptoms of cyanosis, hemoglobinuria, icterus and collapse. At the autopsy are found fatty degeneration of the heart and liver and multiple ecchymoses in almost all the organs. Similar autopsy findings are seen in Buhl's disease in which cyanosis is the chief symptom. In the latter there is a septic infection starting from the umbilicus, or from the bowel (Lucksch), (see Rothler). In Winkel's disease an infection is also probably the cause (b. coli). The umbilical vein is spared. In both conditions, melaena, (symptomatic, see under stomach), may be present (see Nurnberger).

Slight degrees of fatty degeneration are very frequent and usually proved only by the microscope (Eyselein). Functional disturbances do not necessarily result; it has even been considered physiological, depending on nutrition (Wegelin, Hotzen), but higher degrees are incompatible with undisturbed function. In any case in which the cardiac muscle shows plain evidence of fatty degeneration, it is diseased, not in the former sense of a metamorphosis of muscle protoplasm into fat, (fat-metamorphosis, Virchow), but as illustrated in animal experiments (see Leick and Winkler), in which the fat entered from one of the fat deposits; but we must remember that fat can enter a muscle fibre only when its protoplasm permits retention consequent to local disturbance of its metabolism ("degenerative fat infiltration," Herxheimer). On the other hand, Borcher is of the opinion that many cases of fatty degeneration of the heart muscle, are "fat phanerosis," *i.e.*, on destruction of the protoplasm, the invisible lipoids distributed in the normal muscle become visible. The fat content (ethereal extract), of the dry muscle substance may be increased to 26% in phosphorus poisoning; the normal fat content is 11% (Krehl, see Orgler also). Chemical analysis and microchemical staining do not correspond, because the latter fails with fat-protein combinations. We may speak of fatty degeneration to express the pathological fat content of the heart muscle, but as mentioned under pericardium, it is essential to

differentiate carefully between fatty degeneration and adiposis of the heart (fatty heart) which is frequently, although not regularly, a symptom of polisarca, obesity. The heart is often enlarged, (3 times and more), in obese individuals who have muscular strength and abundant circulation, but in weak obese individuals, the heart is usually small. It must be remembered also in the opposite condition, *i.e.*, in atrophy of the heart subsequent to cachexia, that there is sometimes considerable secondary fat proliferation. Fatty tissue, formed by metamorphosis of connective tissue covers the heart, especially its right side. It is lipoma-like, lobulated, overlaps the right rim and the apex, may be from 0.5 to 1.5 cm. in thickness, forces its way between the muscle bundles and fibres, especially those of the right ventricle, and in very advanced stages, is visible through the endocardium, as lipoma-like clumps, spots, or tiny, long, flat, yellow striae and ridges.

But the latter sometimes appear isolated without invasion, and in individuals who do not suffer from lipomatosis (Thorel), a statement which can be substantiated by the author. Fatty heart and fatty liver occur frequently in hard drinkers as well as in chronic gastritis and chronic leptomeningitis (see Fahr). Cardiac function may finally suffer from the fatty overgrowth and infiltration, because in a small heart the constant pressure of fat on the separated muscle bundles and the tax from the added weight, must eventually lead to atrophy and insufficiency. But the large fatty heart may remain capable of functioning for a long time because its muscle is stronger and is able to hypertrophy. When it does fail, we find either no change at all, or simply sclerosis of the coronary arteries (see Hirsch, lit.).

Every experienced pathologist knows that cardiac adiposis causes sudden death following some exertion which taxes the heart, such as running, abdominal compression, overloading of the stomach, chloroform anesthesia, etc. If the fat infiltrated myocardium also shows brown atrophy or fatty degeneration, the wall becomes so seriously weakened and fragile that fatal rupture occurs when sudden strain is put on it or even without strain; it has occurred during sleep. The rupture is usually irregular and ragged as it would necessarily be in this complicated interlaced fibre system.

The clinician calls the fatty degenerated as well as the fat infiltrated and fat covered heart, simply "fatty heart" (Leyden).

### Calcification

Calcification of cardiac muscle fibres is rare; it means "calcium metastasis," (case Roth), in which other organs also show calcium infiltrations (stomach, kidneys, spleen, liver) or degenerative processes combined with

calcification (Hedinger, lit.); chronic nephritis is often present and the general calcium metabolism is disturbed (Hart, M. B. Schmidt). Wiechert (lit.) in his case, assumes there is a toxic necrosis, as in paratyphoid infection, which precedes calcification (see also Tilp, B. Fischer). Hart (lit.), too, is of the opinion that calcification takes place in dead tissue only, and that necrosis is caused in a general sense by infections and toxemias. According to Stumpf, lime may be deposited in a fatty heart (see Siebenmann and lit. by Thorel, Krayn). [For discussion, treatment of certain cases and X-ray recommendation see Cutler, E. C. and Merrill, C. Sosman; Am. J. Roent., 12, 312, 1924.—*Translator.*]

**Amyloid** degeneration plays a minor role. It may involve the intermuscular connective tissue and the vessels; and it may coat the muscle fibres, or penetrate between them with a resulting muscular atrophy (Beneke). It may also affect the epi- and pericardium (see p. 23). Calcification may be combined (Schilder, Hecht; lit. Beneke; see also lit. p. 23).

### Changes in the Myocardium Caused by Circulatory Disturbances

**General Anemia.**—Death from exsanguination is death from acute general anemia. The previously healthy heart muscle is pale, grayish red or grayish yellow. The firm consistency of the acute exsanguinated heart differentiates it from fatty degeneration. In the chronic anemias, with oligemia of the heart, *e.g.*, in chlorosis, there is always more or less extensive fatty degeneration and the organ appears light yellow or clay colored. It is seen in highest degree in pernicious anemia (Biermer).

Changes in the coronary arteries cause local anemia of larger or smaller areas.

The coronary arteries. The right and left spring from the root of the aorta and pass forward beneath the auricles one to the right, the other to the left of the large vessels. They form a vascular plexus in the atrioventricular sulcus. The right supplies the right atrium, the right ventricle, with the exception of an anterior strip, the posterior part of the ventricular septum and part of the anterior wall of the right ventricle. Both coronaries supply the posterior papillary muscle of the left ventricle and the anterior large papillary muscle of the right ventricle (Amnomiya). According to Jamin and Merkel, the branches of the right and left anastomose in a variety of ways, and according to Hirsch and Spalteholz, who injected both dog and human hearts, anastomoses are not only present, but are abundant, although with individual variations. These anastomoses include the finest peripheral twigs in the papillary muscles, subendocardial and subpericardial layers; coarser anastomoses of the main stems are present only in a few places and these especially in the left auricle, so that the coronaries are not anatomic end arteries. Nevertheless the

anastomoses are unable to prevent the formation of infarcts after occlusion of the larger distributing branches. More detailed investigations of their functional capacity in man are much needed. But it is certain that with gradual occlusion of a branch of the coronary artery as occurs sometimes in cicatricial syphilitic aortitis, enlargement of the other coronary artery may take place and a slow, gradual, functionally perfect, collateral circulation develops sufficient to supply an immensely hypertrophied heart. In rare cases there is only one coronary artery, and in an observation of the author in a 47 year old woman, it was the left which was present, (see Abrikossoff, Heitzmann, in reference to the rare origin of a coronary artery from the pulmonary artery).

The coronary veins unite in the atrioventricular sulcus into the coronary sinus (vena magna cordis) which enters the right auricle (coronary sinus valve—valve of Thebesius). Furthermore, it is said that small veins of the inner myocardial layers open directly into the cavities of the heart (von Langer, Toldt). [For review of coronary arterial disease, see Benson, R. L., Arch. Path., 2, 876, 1926.—*Translator.*]

The changes in the coronary arteries in question are (*a*) acute occlusion by emboli, *e.g.*, thrombotic masses from a leaflet of the aortic valve or a fatty degenerated part of the intima of the aorta. This embolic occlusion is rare compared with the following form: (*b*) occlusion from local changes of the arteries, viz., common arteriosclerosis with thickening, fatty degeneration, atheromatous softening and calcification of the intima and rarely of the media; this often begins early in life (Orliansky) and although not rare in young men in mild degree especially in the left coronary artery, (Monkeberg), it is especially common in more advanced age. (See short dissertation on angina pectoris by H. Cohn.) To these local changes, thrombosis may be added with resulting acute occlusion. The lumena are usually open but become narrower along the course of the vessels. Endarteritis, with increasing thickness of the intima may be present in earlier years as a concomitant of syphilitic aortitis, (see under arteries), and may eventually lead to closure of the entrance, while the artery further along in its course is dilated. Furthermore, an acute focal mesarteritis is not a rare occurrence during the course of infectious-toxic diseases such as scarlet fever, diphtheria, measles, eclampsia, endocarditis, pyemia, etc. (Wiesel, see also Scharpff). The anterior descending branch of the left coronary is most frequently affected.

A vegetative endocarditis may penetrate the coronary artery for some distance. Traumatic thrombosis has been observed, as in a case of Eug. Fraenkel after the twisting of a suture around the artery.

For aneurysm of the coronary arteries, see page 4.

Consequences of vessel occlusion.

(*a*) Obstruction of both coronary arteries or the obstruction of one in the presence of an existing closure of the other, causes death, either instantaneous, or in a few hours.

(*b*) When a large branch, or the stem of one coronary artery is acutely occluded, sudden or less rapid death may result, with the symptoms of angina pectoris. These different effects depend on the kind of closure, *i.e.*, whether perfect and instantaneous from an embolus, or one completed by subsequent thrombosis. The condition of the other coronary artery and of the myocardium are other factors. If the other coronary is arteriosclerotic and the myocardium poor with brown atrophy, fatty degenera-

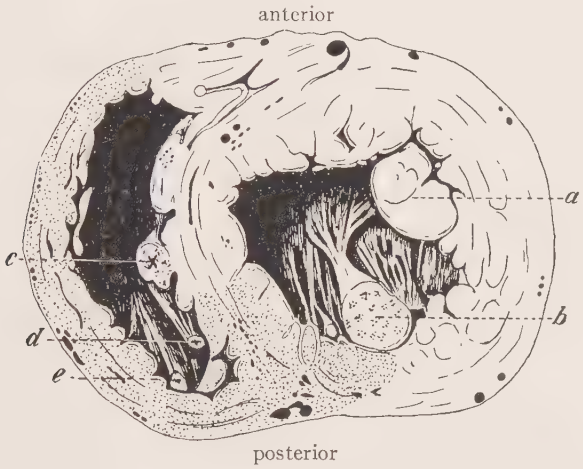



FIG. 20.—Areas supplied by the coronary arteries. Cross section through both chambers, viewed from below. The black dotted area is supplied by the right, the area left, white, by the left coronary artery; a, anterior; b, posterior papillary muscle of the l. ventricle; c, large; d, median; e, lateral papillary muscle of the r. ventricle; b and c are supplied by both coronary arteries; modified from illustr. by Amenomiya (l.c.); $^{9}/_{10}$ nat. size.

tion, fat or cicatrices, then acute occlusion of the right or left causes sudden death (Oestreich, Barth and lit. by Thorel).

The few observations on man do not permit judgment of the effect of acute closure of a healthy left coronary artery with the right one patulous and a perfect valvular apparatus and myocardium. The author's observation of this kind almost equalled a physiological experiment. A laborer, very sturdy, 35 years old, worked in the morning as usual; at 1:00 P.M. he showed sudden dyspnea, quickly followed by severe pulmonary edema, resulting in death at 7:45 P.M.; autopsy revealed: closure of the left coronary artery by a small, loose, firm, embolus in the anterior descending ramus, from which softer, loose, thrombotic masses extended up to the origin of the circumflex ramus; a flat thrombus the size of a lentil with roughened surface as though torn off, lay close above the posterior leaf of the aortic valve. There was globular distension of the left ventricle

(cardiac paralysis), with the right ventricle in comparison small, firm, valves intact, good musculature (also microscopically); both lungs flooded with edema.

(*c*) If a small branch is occluded, ischemia of the part supplied is the consequence. At first the consistency remains normal, but its color becomes steadily lighter, until the tissue dies, when it becomes clay colored, gray or yellowish and usually firmer and drier than its vicinity (coagulation necrosis). This is the familiar anemic necrosis, or anemic infarct. These necrotic areas may show map-like figures of varying shapes caused by the distribution of the vessel.

FIG. 21.—Infarction and perforation of the wall of the left ventricle with vegetative mitral endocarditis. L. H. #89.

Microscopically, at first, the outlines of the fibres are still preserved and the cross striation intact, but with the exception of parts of the connective tissue, there is no nuclear staining. Then follow degeneration of the necrotic muscle fibres, with waxy or hyalin vacuoles, and lumpy or granular disintegration. In some places, the muscle fibres show fatty degeneration. In the interstices between the necrotic muscle fibres are found fresh foci (a few days old) of fat-containing leucocytes. Some muscle fibres are much swollen.

At the periphery of the foci, is the red line of hyperemia. Blood extravasation occurs from the neighboring vessels (hemorrhage). If the necro-

tic area itself becomes saturated with blood as in smaller foci, it constitutes the dark red hemorrhagic infarct, which later becomes brown or rusty in color. Often, a small, angular, yellow seam of fatty degeneration is present between the red edge and the clay colored focus, *i.e.*, in the peripheral parts of the anemic area, since at least some blood percolates into this region from the hyperemic surroundings; when the anemia is complete, the inevitable result is necrosis.

What becomes of anemic infarcts? First they soften secondarily and become friable from serous saturation from the neighboring vessels (soften-

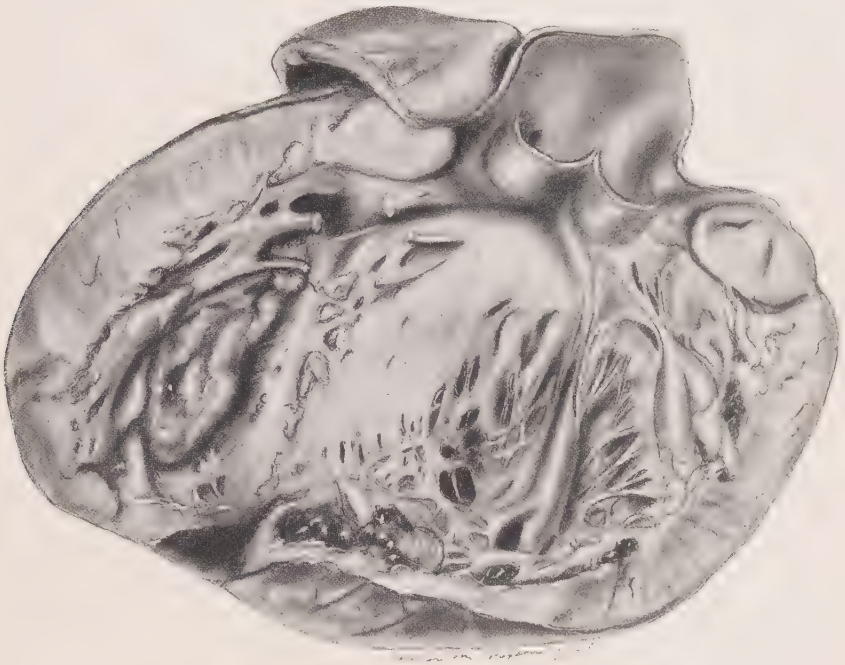


FIG. 22.—Infarction of the heart muscle. Thrombosis of the anterior coronary artery. The infarction present toward the apex of the left ventricle covered by thrombus. Such lesions heal occasionally but later form a so-called cardiac aneurysm from the stretching of tissue less resistant than the original muscle. L. H. #16.

ing of the heart, or better, myomalacia). Rupture at this time is relatively rare, but perhaps there is a small, irregular tear, the edges of friable myocardium penetrated with blood. The epicardium is bulged outward by bluish red, translucent, blebs of blood.

But when the soft area bulges as a whole (acute cardiac aneurysm) rupture is quite common.

An acute dissecting cardiac aneurysm is developed when only the inner subendocardial layers of muscle are torn; the blood penetrating the myocardium separates the muscle layers, perhaps for a considerable

distance. The cardiac surface then bulges outward like a hemisphere. Perforation may occur at the apex of this prominence, but when there is extensive dissection, tears occur at the cardiac base.

Organization of the infarct is much more frequent, however. Vascular granulation tissue from the reacting interstitial tissue of the neighborhood penetrates the necrotic area as the disintegrated material is removed by cells and absorption (see p. 9). The end result, when the change to firm, satiny, fibrous connective tissue is completed, is a scar (myocardial cicatrix). While it is forming, the process should be called fibrous myocarditis, or, better "fibroplastic myocarditis" (see fig. 26). The areas which are to become connective tissue first appear grayish red and slightly sunken, later they shrink more and more into a non-vascular, white, firm cicatrix with brownish spots. Microscopically, the yellowish brown granules are contained within connective tissue cells which are rich in protoplasm and varied in shape (phagocytes). The pigment owes its origin chiefly to blood coloring matter from the hemorrhage; it gives the iron reaction, but may be derived in part from the pigment of destroyed muscle fibres, in which case it is darker brown and gives no iron reaction. In the vicinity of the scars are fat deposits, hypertrophic muscle fibres, fibres with remarkably large nuclei rich in chromatin, sometimes also muscle giant cells (attempts at regeneration?). The scars contain abundant elastic fibres, (see Faber and others).

If the scars are numerous, the heart muscle, on section through the ventricular wall, appears spotted or striped, tiger-like, color flecked; if old it is spotted white and brown; if more recent, it is grayish red; fresh changes are clay colored with an outside yellow zone of fat infiltration and a hyperemic edge alternating in the same specimen with typical hemorrhagic infarction.

Should many scattered small necroses occur which undergo cicatrization, we have a "disseminated fibrous myocarditis." Hardening of the heart muscle (myocardial cirrhosis) and hypertrophy are frequently combined, doubtless for purposes of compensation. This is often seen in large senile hearts.

Scars are much more frequent on the left side (left coronary artery) than on the right (see heart cicatrices and consequences on p. 68).

### Myocarditis. Inflammation of the Heart Muscle

According to the part chiefly affected, we may consider a parenchymatous or muscle type, and an interstitial or connective tissue type, the latter either acute or chronic in nature. But it is clear that the muscle fibres must always be changed in interstitial myocarditis, and conversey, in parenchymatous degenerative inflammation there is always change in

the interstitial tissue. For this reason it is well to speak of a predominantly parenchymatous and a predominantly interstitial myocarditis.

### Parenchymatous Myocarditis, Predominantly Degenerative Myocarditis

This type develops acutely, and appears as cloudy swelling, which either regresses or becomes fatty degeneration. The interstitial tissue is involved in varying, but usually mild, degree, and shows a small round cell infiltration. It is merely hair-splitting to argue over "parenchymatous myocarditis" or "myocarditis with marked predominating parenchymatous involvement" (Ribbert). There are still other forms of acute parenchymatous degeneration, such as "vacuolated or hydropic degeneration" in which droplets form in the cell protoplasm; hyalin degeneration; granular lumpy disintegration; loss of cross striations, with glassy and hyalin droplet appearance analogous to waxy degeneration (see under muscles), such as von Flessinger and Roudowska observed, especially in preagonal cardiac arrhythmia of the atrioventricular bundle. In anemic necrosis (p. 58), there are reactive growth of connective tissue and gradual absorption of dead masses to fill out defects in the loose scar tissue. Fatty degeneration frequently combines with the forms of degeneration just mentioned, especially in pharyngeal diphtheria, protracted scarlet fever (see Stegemann), typhoid fever, in which the heart is often remarkably flabby, pneumonia, (see Liebmann) in which the right ventricle is only exceptionally affected (Fulci). The fat is focal or diffuse, and appears not only during the height of these diseases, but also during convalescence; it may cause severe enough cardiac disturbances to cause death from cardiac paralysis. As causative factors we should consider the blood changes present in infectious diseases and fevers, *i.e.*, diminished oxygen, the entrance of bacterial toxins, etc. The muscle may become so fragile that it is properly called inflammatory softening, but in children's hearts the changes in consistency are usually not so marked. As long as the cloudy swelling is present, the heart muscle is somewhat fragile, and usually cloudy grayish red, but with increasing hyalin degeneration it becomes paler and grayish or whitish yellow as though cooked.

Enlargement of the cavities is frequent, especially of the left (see Sorensen), but thrombus formation as well as embolism is rare (Deguy and Weil, lit. by de la Chapelle).

In diphtheria, the myocardial findings are inconstant and varied, probably because of qualitative differences in the diphtheria toxins (Fahr); they also vary according to earlier or later stages under investigation, but the severity of the infection does not necessarily correspond to the histological changes (Huebschman, lit.). While Birch-Hirschfeld, Leyden,

Romberg and others consider an interstitial infiltration as primary, although it is not to be seen before the 9th to the 15th day of the disease (Hallwach and Tanaka), others consider the predominant factor to be parenchymatous, *i.e.*, fatty degeneration, the frequency of which is recognized by all (see Hotzen, Rosenbach, Schemm, and especially Ribbert). Waxy degeneration is also found, and Tanaka emphasizes parenchymatous lumpy disintegration. Eppinger (toxic myolysis), Moenckeberg, Fahr (myolysis), and others, and recently Huebschmann, have reported primary parenchymatous lesions. From all this we may assume that diphtheria toxin injures first and chiefly the muscle fibres, which show either a finely sprayed fatty degeneration of comparatively slight importance as long as nuclei and cross striation persist (Monckeberg), or more severe

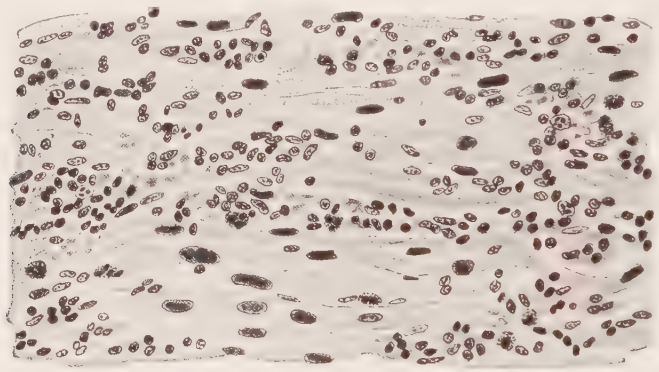


FIG. 23.—Acute myocarditis in pharyngeal diphtheria showing gaps of disintegrating muscle fibers with well preserved fibers containing large dark nuclei; the former invaded by lymphocytes, leucocytes, isolated eosinophiles and fibroblasts with pale elongated nuclei; from a child, cardiac death; × 300.

swelling and lumpy disintegration. These changes appear alone or in combination. Secondarily, there is usually a round cell infiltration which may be quite marked (see above). Plasma cells, and sometimes eosinophilic cells, also make their appearance (Tanaka Wulffius). In severer cases, the destruction of muscle stimulates granulation (fig. 23), with the final result expressed in a fine, loose connective tissue (see Anitschkow also). Very rarely, microscopic dense scars are found, (Huebschmann). The muscle has a tendency to acute dilatation on account of numerous foci of loose connective tissue. These, and the other fresh myocardial changes are sufficient to explain the acute "cardiac death" so frequent in diphtheria. Indeed the heart, especially the left, is often dilated with but slight anatomical changes. Both thrombosis and embolism are relatively rare. The transmission system may remain free of changes, or may also be involved (Tanaka, Rohmer, Heilhecker).

Heller first described regenerative processes in the diphtheria heart consisting of enlargement and better staining of nuclei, segmentation of nuclei, hypertrophy of fibres and multiplication by lateral division of myogenous cells and muscle bands. These findings were verified by others (Frenzel, Huebschmann, compare, with the per contra, Anitschkow).

### Predominantly Interstitial Myocarditis

#### (*a*) acute interstitial myocarditis (fig. 25)

A sharply localized, and a more or less diffuse form may be differentiated. The former develops by continuity from an ulcerative endocarditis, thus forming a heart ulcer (comp. fig. 9) or by the extension of a suppurative pericarditis into the myocardium, or, much more frequently, from infectious emboli in ulcerative endocarditis, pyemia, etc. The organisms are usually staphylococci, especially from osteomyelitis, but streptococci, sometimes pneumococci, rarely gonococci (Councilman) all may reach the heart muscle through the blood from the coronary arteries. A suppurative inflammation is the usual result.

Cloudy speckled foci develop wherever bacteria lodge which is often in the vessels. These foci show cloudy swelling and necrosis, and further out, there is fatty degeneration, changes which can be considered as progressive death of tissue due to diffusing bacterial toxins. The necrotic masses are usually surrounded by a reactive zone of leucocytes (fig. 25). When pus cells enter a necrotic focus, an abscess is formed.

Although this course of events is the more frequent, the process does not necessarily develop into a suppurative myocarditis. The bacteria or their toxins may cause only necrosis with peripheral leucocytic infiltration, for the virulence of the bacteria may be diminished. This is often seen in pneumococcic endocarditis. Tiny scars may form from reparative connective tissue proliferation. There are also cases in which purulent liquefaction does not occur, but cellular infiltrates of proliferating fixed connective tissue cells, lympho- and leucocytes, eosinophiles, etc., gather without causing marked changes in the muscle fibres; this constitutes the true interstitial foci. In other cases, it is very difficult to decide if the involvement of the muscle fibres is primary or secondary, (hyalin degeneration, necrosis). The productive inflammation is very marked in some foci, and we see polymorphous fibroblasts and much connective tissue.

Aschoff first described a type of myocarditis, frequently, although not always, accompanying articular rheumatism (polyarthritis rheumatica). In this type are found inconstant, nodular, perivascular foci within the interstitial tissue, usually recognizable only microscopically, but occasion-

ally, macroscopically (Sternberg). They are called Aschoff's nodules, and are composed of peculiar, large giant cells with large nuclei of connective tissue origin, which are grouped in a radiating or fan-like form intermixed chiefly with lymphocytes, but also with eosinophiles and plasma cells. The centers of these nodules become necrotic and later are partially or completely fibrosed. According to the opinion of many authors, (Thorel), this rheumatic myocarditis, (Eugene Fraenkel, lit.) is a specific disease of the heart muscle. The nodules which select by preference the richly vascular subendocardial layers may threaten destruction to the numerous branches of the conduction system. The importance of diplo-streptococci which were cultivated from the heart blood of cases

FIG. 24.

FIG. 25.

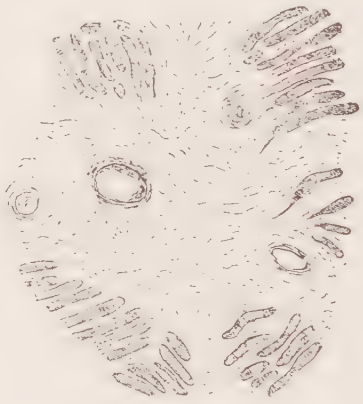


FIG. 26.

FIG. 24.—Anemic necrosis of a small portion of muscle fibers; slight infiltration of leucocytes into the interstitial tissue; (low power).

FIG. 25.—Small cardiac abscess; in the center, long black masses of bacteria surrounded by a light necrotic zone and beyond this a wall of leucocytes; puerperal pyemia; Gram stain (low power).

FIG. 26.—Scar in the myocardium due to sclerosis of coronary artery; four vessels lie in the fibrous tissue; the upper three, with thickened intima are arteries. The fibrous tissue is lost between the adjoining muscle fibers (low power).

of rheumatic polyarthritis in some instances, and which, in animal experiments, caused necrotic inflammatory foci with a tendency to form scar tissue, is still doubtful (Eug. Fraenkel), especially in view of the experiments of de Vecchi (lit.), who succeeded in developing perivascular myocardial foci with sterile blood from patients with acute articular rheumatism. Their resemblance to Aschoff's nodules were pointed out by the author. In both articular rheumatism (rheumatism nodosa), and in chorea minor, which is related to the former, the presence of subcutaneous nodules to the size of hazel nuts (rheumatic nodules) has been known for a long time. They are found not only in the vicinity of the swollen joints, but also in other places visible to the eye, and are analogous to those in

the myocardium (see Fahr). Similar small macroscopic nodules have been found on the galea aponeurotica (Tilp, Jacki, lit.).

Interstitial inflammatory foci in the myocardium are also found frequently in other endocardial and valvular lesions.

In pharyngeal diphtheria, microscopic interstitial inflammatory foci are often found in large numbers (see p. 61), and occasionally also in other infections. Staubli speaks of eosinophilic myocarditis in rabbits with the trichina heart (compare in man, Hubner, Knorr and Simmonds "myocarditis trichinosa"). Diffuse interstitial inflammation with the formation of fluid exudate and cellular infiltration is rare in infectious diseases, but is occasionally seen in scarlet fever and in pharyngeal diphtheria; extensive pale yellow foci may also be present.

Isolated, acute or subacute diffuse interstitial myocarditis is rare; when it occurs, there are large glassy yellowish to grayish white foci in the myocardium. The author saw two cases which looked like leukemic infiltration; there were washed-out figures in the myocardium, which extended so far that little normal musculature was left. The heart is usually dilated and considerably enlarged; sudden death frequently ends the condition. Other organs show few abnormalities; the clinical course is peculiar (Pal); it prefers younger individuals. The etiology varies. In a case of the author, there was an infected, but rapidly healing, burn; in another case, pus developed in the incision after operative removal of a tuberculous cervical lymph node. In Wolf's case, there was an unimportant lesion of the elbow; in Aschoff's case, one of the hand; a facial carbuncle which healed after incision was present in a case of Sellentin (lit.). In a case of Zuppinger, a child had a phlegmon of the foot; trauma and other obscure causes have also been recorded (lit. in appendix). Probably the toxic action of bacterial products is concerned, for bacteria themselves were never found in the foci. Histologically, the findings are not uniform; in some, the mildness of the parenchymatous changes is emphasized (for instance, the cases of Sellentin, of Aschoff); while in others we find more marked fatty degeneration, and disintegration to complete atrophy of muscle fibres. There are undoubted attempts at regeneration with proliferation of free muscle nuclei (see Wolf) and myogenous "wandering cells" (see Saltykow). There are muscle giant cells, epithelioid cells, leucocytes and lymphocytes, eosinophiles, and other cells. The inconstancy of the parenchymatous changes points to the interstitial changes as the essential, although L. Cohn considers hyalin degeneration the primary lesion.

Abscesses sometimes appear in enormous numbers as globular or elongated striae and foci. A hyperemic or hemorrhagic halo surrounds

small miliary abscesses which may often be picked out with the point of a knife.

The areas of predilection, as for all focal myocarditis, are, according to Koster, in the papillary muscles, especially the left, where there are small striae, or more rarely, globular knobs on their apices, in the lower two-thirds of the surface of the left heart, and on its posterior surface more toward the middle. The anterior right papillary muscle is next preferred. Other favorite places are the subepicardial muscle layers, and for this reason, Koster, advises slicing fine sections parallel to the surface to find them more readily. Their size is usually small, but occasionally foci as large as a pea develop by confluence, rarely, larger ones are found. If the infectious emboli are larger, inflammatory and simple mechanical sequellae are combined and anemic infarcts border on abscesses, so that the former finally suppurate. Abscesses have been known to heal, as the bacteria die and the pus cells disintegrate and are absorbed. Granulation tissue invades and covers the focus which changes to a fibrous scar (myocardial scar). The necrotic foci may be dealt with in the same way. In other cases, the abscess becomes encapsulated. Calcification of the thickened pus is rare.

The consequences directly due to the abscesses vary according to their location and size: (*a*) If the focus lies under the epicardium, there is danger of pericarditis (purulent, fibrino-purulent); (*b*) if located in a papillary muscle, separation and acute insufficiency of the valve may occur; (*c*) if directly under the endocardium, it may break through and release emboli, especially into the spleen and kidneys, or it may produce ulcerative myocarditis. If blood tunnels into the ulcer, it distends in a short time and forms an acute ulcerative cardiac aneurysm which may progress to fatal rupture. On p. 32, was described another form of cardiac ulcer from extension of an ulcerative valvular endocarditis to the cardiac wall; from these also, acute cardiac aneurysms develop; (*d*) if the abscess, *i.e.*, ulcer, is located in the ventricular septum, (usually in the upper part), a communication between the ventricles may develop; (*e*) in other cases, the ulcer bulges toward the right auricle or the pulmonary artery. Rupture or thrombus formation outside of the aneurysm sometimes occurs and may cause pulmonary embolism.

Ulcerative cardiac aneurysms may become chronic, in which case the wall contains a scar.

### CHRONIC FIBROPLASTIC INTERSTITIAL MYOCARDITIS; FORMATION OF SCAR TISSUE

We must differentiate (1) the rare, independent, chronic productive myocarditis; (2) the very frequent secondary productive myocarditis

which follows an acute process—usually a myocardial necrosis and at times aseptic cardiac wounds (lit. by Cevidalli and see lit. p. 83), as a reactive reparatory attempt. In both cases, scar tissue may form (cicatrix, see circumscribed fibrosis of the myocardium).

If the process has not completely ended, which cannot be decided as a rule macroscopically, we are justified in speaking of fibrous myocarditis, or, better, "fibroplastic" myocarditis.

This formation of scar tissue ends in the development of calloused connective tissue, rich in elastic fibres which evolves by a modification of granulation tissue and becomes established within the cardiac wall in

FIG. 27.—Myocardial cicatrices; cross section through the anterior end of the ventricular septum; the white streak is the epicardium; natural size.

FIG. 28.—Fibrosis of the tip of a papillary muscle.

place of, and at the expense of, the musculature. These changes are best recognized by flat sections through the heart walls. At first, there is a red, somewhat soft, depressible focus in the musculature; after cicatricial transformation, this is grayish red or pale brownish to white, resembling asbestos, tendinous and shiny; it sounds gritty under the knife, and is depressed below the section surface. The foci usually are flat, but are sometimes nodular (fig. 27).

An independent, insidious, chronic productive myocarditis has been described following articular rheumatism, typhoid fever, puerperal fever, and has also been accepted by many clinicians in relation to other infections, such as measles and pneumonia, especially in children (lit. by Thorel; see below as to syphilis). It is probable also that an acute myocarditis

may run a protracted course, and in this way, it is possible to have an occasional chronic myocarditis in those infectious diseases in which we more frequently find acute myocarditis.

There are other processes in which a productive myocarditis is a secondary complication as in: (*a*) Acute myocarditis, especially an abscess, but, in any given case, it may be merely acute parenchymatous degeneration (see p. 61). (*b*) Scar tissue in the outer myocardial layers may follow a chronic pericarditis. (*c*) A parietal endomyocarditis following valvular diseases. A conus stenosis can thus be developed in the right heart, rarely in the left, followed by true stenosis with subsequent dilatation and hypertrophy. Often the papillary muscles, especially the left, or separate trabeculae become fibrosed (fibrous myocarditis or papillary fibrosis) for which mechanical factors are sometimes responsible (pulling). Valvular insufficiency may result. (*d*) Necrosis of the myocardium is most frequently caused by changes in the coronary vessels, (arterio-sclerosis, endarteritis, thrombosis, embolism). These changes in the intima are not found in the larger vessels alone, but, quite frequently indeed, in the small intermuscular branches of the coronaries, as well as in the arching twigs which enter the large papillary muscles (see p. 55). The most common causes of these conditions are arterio-sclerosis and syphilis. The most minute, and the largest cardiac scars are met in this connection. Sometimes there is a syphilitic mes- or end-aortitis, and sometimes there are true gummata in the pericardial adhesions. This was seen by the author in a man 35 years old, in whom the generally dilated and hypertrophic heart showed such a high degree of scar tissue formation that the wall (also that of the right ventricle), was occupied by scars the size of a dollar; the beginning of the aorta was much distended and there was advanced arterio-sclerosis. (*e*) Not all cases of fibrous myocarditis in syphilitics can be charged to vascular changes; there are some in which toxic action on the muscle fibres themselves must be considered as the primary cause. The destruction of muscle fibres is followed by reparatory connective tissue overgrowth. On the other hand, there is a primary chronic interstitial myocarditis in syphilis, with or without the formation of gummata, (cases of Buschke and Fischer in congenital lues, but only the latter case is characteristic; in a third case, scar tissue formation with aneurysm followed the disappearance of gummata after specific treatment). Experimental chronic myocarditis was studied by Fleisher and L. Loeb, (lit.).

**Consequences of Cardiac Scars.**—If the scar surrounds the conus pulmonalis or the aorta like a ring, it leads to stenosis of these parts, but this is an infrequent occurrence. On the other hand, an area with a large scar may be bulged outward by the blood pressure and thus form a

chronic cardiac aneurysm; (aneurysma cordis partiale, Rokitansky). This must not be taken too literally; most of such aneurysms are not especially easy to recognize but become noticeable only on section of the heart. Nevertheless cases do occur in which a large spherical bulging the size of a fist and larger can be seen (transverse bag-heart). The aneurysmal wall, when large, consists only of scar tissue, sometimes calcified. On the outside, there is usually a calloused thickening of the epicardium, and not infrequently, bands or flat adhesions join both pericardial surfaces.

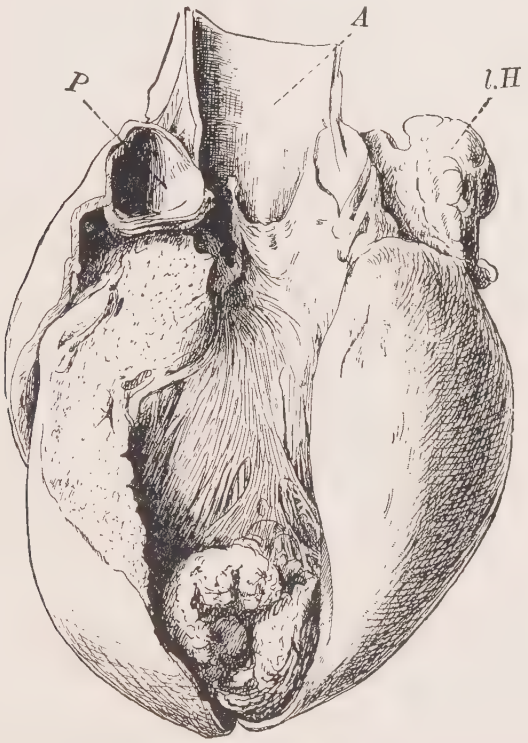



FIG. 29.—Typical chronic cardiac aneurysm anterior, at tip of left ventricle; the wall cicatricial, calcified and thinned; in the aneurysm a parietal thrombus with central softening; A, aorta; P, pulmon. art.; l.H, left auricle.

Frequently, massive thrombi with ribbed layers collect within the aneurysm (these are also called parietal thrombi since they are attached to the wall), and these sometimes soften in their interiors, or they desiccate and become of horny hardness (fig. 29). Embolism is frequent (fig. 30), and organization is rare.

Rupture of a partial cardiectasia is relatively rare, because cicatricial thickening of the endocardium and frequently of the pericardium protects; laminated parietal thrombi also protect. Nevertheless, in any group of spontaneous cardiac ruptures (see p. 4), those due to aneurysm are quite

frequent. The favorite location of aneurysms is in the anterior wall of the left ventricle, near the apex (anterior descending branch of the left coronary artery, which also is the sole supply to the anterior large papillary muscle of the left ventricle). It occurs chiefly in old men (Strauch).

The chronic aneurysms which develop by scar formation in the septum bulge to the right; other localizations are rare.

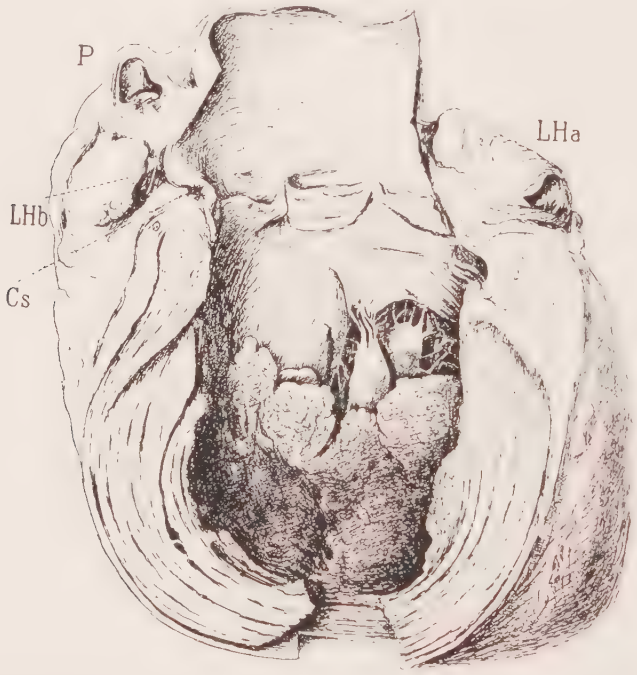



Fig. 30.—Cardiac aneurysm filled with immense thrombus partly laminated, horny and firm; the rest of the wall of the left ventricle adjacent to the aneurysm cicatricial and thin; partial adhesions of the pericardium. The opened left ventricle is shown. LHa, left auricle, cut; a portion to the right of the cut (LHb); Cs, left coronary artery, P, pulmonary artery. Sclerosis of the coronaries; weight of heart 910 gms. Man 60 years old with chronic nephritis (large white kidney) died of uremia. Embolic gangrene of both feet; ½ nat. size.

## Appendix. Fragmentation and Segmentation of the Myocardium

This is probably an agonal change which develops under the most varied conditions; it can be recognized with certainty only by the microscope. In a general way, it consists of transverse separation and splitting of the cardiac muscle fibres into small fragments, causing them to appear chopped up, or torn jaggedly. Sometimes the edges of the transverse tears show longitudinal splintering or unraveling (primitive fibrillae!). The tears and separation occur not only within the cross stria (p. 48), but anywhere along the continuity of the fibres, (true fragmentation); fracture lines through nuclei are rare.

According to Jordan and Bardin, segmentation and fragmentation are but different degrees of the same process.

This change is found most frequently in the left ventricle, especially marked in the papillary muscles and inner layers. It is rarely general in distribution.

These findings have often been made in sudden death (hanging, asphyxia, drowning, execution, etc.), in which the heart muscle was perfectly healthy. On the other hand, it is found in the most diverse diseases, where perhaps septic processes are prominent. We must assume, (*a*) when the muscle was healthy, that the short agony during sudden death suffices to fracture the heart mechanically by violent spasmodic contractions, while (*b*) nutritive disturbances of various kinds (among them senile atrophy, see Wideroe), may diminish the firmness of the muscle sufficiently to permit the last, more or less spasmodic, contractions, which need not be especially violent, to cause fragmentation. The change therefore cannot be considered of diagnostic importance, *e.g.*, in the causes of death, from a suddenly acting force. Its frequency increases with progressive age. It is absent in the newborn. The fragmented heart muscle may also show fatty degeneration.

Giese's statements, that it is experimentally possible to produce typical fragmentation by putrefaction, which would mean that fragmentation is actually a cadaveric condition, were not substantiated by Stamer (lit.), nor can he subscribe to the opinions of Tawara and Aschoff that mechanical post mortem procedures cause full development of fragmentation which was but begun during agony; indeed, like the author, he supports the opinion of Recklinghausen of the agonal cause of these changes (see also Lissauer, experiments, lit.). The dissolution of cardiac muscle fibres, occasionally observed in putrefaction, is distinct from fragmentation and segmentation.

The designation "myocardite parenchymateuse segmentaire" (Renaut), is poorly chosen, since the process has nothing to do with inflammation.

### Changes in the Size of the Heart

The normal heart is approximately the size of its owner's fist (Laennec); the average weight in women is about 250 gms., in men, about 300 gms. (See more details about its weight at different ages by Thoma, W. Muller, exact methods of weighing, and the data and charts of Vierordt, also Wideroe for mass conditions of the heart in pathologic cases; and Kirch in reference to the laws of alteration of internal size of the normal and pathological heart.) While there is no noteworthy difference in the thickness of the ventricles of the heart of the fetus, in adults (according to Krause),

the right ventricle is 0.5 to 0.7 cm., the left 1.1 to 1.4 cm. These measurements, however, vary within rather wide margins, as do the weights and measurements of the hearts, *e.g.*, of soldiers (see Fahr). In hypertrophy, the left ventricle may be 3 cm. thick in the vicinity of the mitral valve. When giving measurements, it is necessary to state where they were taken, and the trabecular substance, and pericardial fat must be deducted.

Post mortem rigor of the heart which causes contraction (pointing and hardening) must also be taken into consideration when judging the thickness of walls and the size of cavities. It appears early, even in one to two hours, (Strassmann, Fuchs, Volkhardt, Aschoff), and complicates the problem of deciding in which phase of heart action death occurred. It may, however, be considered as settled that the heart always dies in diastole (animal experiments, see Rothberger, Eckstein), Usually the left heart at autopsy is almost completely empty (systole). while the right heart is filled, (half diastole, midway between diastole and systole); if the rigor subsides, and the blood in the left auricle remains fluid the left ventricle may fill by suction. As a whole, the heart then becomes wider, flabby and compressible. As a rule, the right ventricle and auricle in the cadaver contain much blood, which is forced in death from the contracting arteries into the veins. This condition neither excludes death from cardiac paralysis, nor does it prove death from asphyxia. Generally speaking, in death from cardiac paralysis we expect distension and globular enlargement of the left ventricle (comp. observation on p. 57), while in death from asphyxia, *e.g.*, in embolic occlusion of the trunk of the pulmonary artery, the right ventricle is filled to the maximum. In severe parenchymatous degeneration of the muscle, as in sepsis, chloroform poisoning, (also in poisoning by phosgene gas, see W. Koch), the rigor may not develop or may quickly resolve in decomposition. Decomposition and adsorption, (see p. 51), may cause fluid blood to disappear from the heart cavities.

**Decrease in Size.** When congenital, it is called cardiac hypoplasia. More marked degrees are rare. Slighter degrees are seen in combination with poor arterial development (hypoplasia), narrow aortic system and chlorosis, (Virchow). It is still a question which is cause and which is effect.

Another much debated question is whether the narrowness of the aortic system is primary. Suter denies it, while Scheel admits it, in the sense that a relatively narrow aorta is present in the years of puberty, because the growth of its lumen does not keep pace with general development. Strasburger proposes calling general aortic narrowness, incomplete dilating power of the aorta. The author supports the theory of a congenital narrow aorta with thin walls but increased elasticity often com-

bined with a tendency to fatty degeneration of the intima—an "aorta angusta" in which a small heart is also found. Frequently, the endocardium of the left ventricle is milky, cloudy, and thickened. Aortas are seen of but three to four centimeters in circumference in the pectoral area, and we may assume with Burke, that in youthful individuals, a left cardiac hypertrophy with later dilatation and arterio-sclerosis, especially of peripheral vessels, are the consequences (see Apelt, Strauss, v. Ritook, Viesel, etc., also Kani, Rossle, Herxheimer, Romberg, Kulbs, Westenhofer, Sternberg, lit.). Bartel, and the author also, saw aortic hypoplasia in status lymphaticus (see Stoerk, Bauer, lit.). Others fail to see such relations, (L. Kaufmann, Jaffe, and Sternberg), and believe that the narrowness is misleading, being caused by the greater elasticity of the vessel and its post mortem contraction. Bauer, however, thinks that the narrow aorta is part of the symptoms of constitutional hypoplasia as we find it in status lymphaticus, (see Bartel also).

The width of the aorta of the adult male in the ascending part is 6 to 8 cm., in the pectoral part 4 to 5 cm., abdominal part 3.5 to 4.5 cm. It is less wide in women.

An acquired diminution in size is called atrophy. The muscle fibres themselves become smaller. In general senile atrophy, in phthisis, in the cachexia of carcinoma, etc., the weight of the heart may be reduced to 150 gms. and less, as a consequence of general malnutrition.

Then atrophy is often combined with brown pigmentation. During life, we frequently see in x-ray pictures, a small, elongated cardiac shadow combined with a long small aorta and a low position of the diaphragm (lit. by Kulbs).

In a girl 18 years old with advanced intestinal tuberculosis, we saw a heart weighing only 100 gms. In very old men, we find an atrophic brown heart which always shows connective tissue hyperplasia especially in the auricular myocardium; this belongs to the picture of general senile marasmus. The large senile heart depends, as a rule, on secondary hypertrophy with emphysema, arterio-sclerosis, etc. In sturdy old men, such a heart may function perfectly.

**Increase in Size.**—This is caused by hypertrophy and thickening of the walls, or dilatation of the cavities, or both together. We understand by hypertrophy, an increase in the mass of cardiac muscle caused by increased activity. We differentiate (*a*) simple hypertrophy, thickening of the wall without changes in the cavities, and (*b*) eccentric hypertrophy, also called "hypertrophy with dilatation."

Concentric hypertrophy, in the sense that the addition of muscle mass narrows the cavity, occurs only rarely in adults (Horvath, see also Kirch); usually such a picture is only the effect of rigor mortis. On the other hand,

the fetal heart does show concentric hypertrophy with thickened walls and small cavities, since it must not only keep up the circulation of its own body but must overcome the resistance of the fluid medium, *i.e.*, the amniotic fluid (Miura). According to Parrot, this condition persists to the 10th year (for congenital hypertrophy see p. 96).

False hypertrophy in a clinical sense is the enlargement which takes place at the expense of the musculature, which is thin, *i.e.*, dilated. We can speak of it pathologically-anatomically, if, for instance, tumors or an echinococcus cyst, cause cardiac enlargement.

For hypertrophy to occur it is necessary to have abundant nutrition; the muscle is reddish brown, often somewhat glassy and of the consistency of rubber.

The muscle fibres are increased in volume and thickness (Goldenberg, Tangl, Romberg and others); perhaps also an increase of fibrillae takes place. The nuclei enlarge (multiplication, division is absent, see Wideroe). [According to Karsner, Saphir and Todd, there is little hyperplasia, most of the increase in size is due to hypertrophy. There seems also to be a maximum beyond which the fiber cannot increase in size. In atrophy there is both diminution in numbers and size. Am. J. Path., 1, 351, 1925.—*Translator.*]

The interstitial tissue, especially its content of elastic fibres, is also increased (Melnikow-Raswedenkow). According to Dietrich the cross striae and cement lines are further apart.

### Development of Hypertrophy and Dilatation

Hypertrophy and dilatation are the results of maladjustment between the work to be accomplished, and the primary mass of functioning muscle substance. Such disproportion is caused, *e.g.*, by stenosis of the ostiae which causes chiefly eccentric hypertrophy, or by valvular insufficiency, which causes chiefly dilatation. In hypertrophy, this disproportion is overcome by muscular growth supported by abundant nourishment; the balance is maintained, at least for some time, through the utilization of reserve power (O. Rosenbach), perhaps even through gain of new reserve energy. Hypertrophy results from increased work of the heart, but with insufficient nutrition, or with steadily increasing work, the reserve power is exhausted, (see Schluter), the muscle yields, and the cavity distends.

According to Horvath, the actual cause of hypertrophy is excess of muscle tonus, *i.e.*, the muscle is more markedly distended and under greater tension. In general, hypertrophy is more frequent in youthful, well nourished individuals while dilatation occurs in older, poorly nourished individuals.

In children, hypertrophy develops very quickly under certain conditions, for the growing young heart with its large capacity for accommodation, offers in its normal growth, the prototype of physiological compensatory hypertrophy.

If progressive hypertrophy fails, early or late, the regressive state sets in, "decompensation" and dilatation begin, and the overworked, insufficient muscle undergoing vacuolation, granular and fatty degeneration (secondary fatty heart), will fail suddenly or gradually; or, the hypertrophic heart muscle ceases it work without an anatomically recognizable cause as far as our present means can determine. Death is caused by cardiac paralysis quickly, or with increasing pulmonary edema (respiratory paralysis).

Krehl and Romberg in explaining insufficiency of the hypertrophic heart muscle probably lay too much stress on secondary complicating interstitial and muscle changes, and Tawara and Aschoff, Stein and others have opposed their view. But whether failure of an hypertrophic heart can be explained by non-cooperation of the muscle fibres of the stimulus conducting system is still doubtful (see Low, lit.). In opposition to Stadler, who explains insufficiency in valvular disease by myofibrosis, (Dehio), *i.e.*, a progressive connective tissue proliferation, and against the supposition of Albrecht, that the hypertrophic heart always shows severe changes, it must be emphasized that sometimes no pathological change of any kind can be demonstrated in a paralyzed heart muscle. At all events, it is questionable whether the occasional positive findings which Babes reports (connective tissue increase; but different from the connective tissue cicatricial substitution in the diphtheria heart, see p. 61) should always be viewed as important in cases of cardiac death, but we might accept it for extensive fatty degeneration (lit. by Schluter, Eugen Albrecht, Lissauer and others, C. Hirsch, Fahr).

**Special causes of hypertrophy and dilatation are:** (*a*) In the right heart, pulmonary changes with difficulties in circulation through the pulmonary artery, especially from focal narrowing or obliteration as in emphysema, chronic interstitial pneumonia, left heart lesions, bronchial catarrh, bronchiectasis, anthracotic induration of the bronchial lymph nodes which causes narrowing of bronchi and pulmonary vessels, especially veins, pleuritic exudates, pneumothorax of some duration (Bruns), scarred adhesions of the pleural layers, thoracic distortion, especially kyphoscoliosis which leads to decrease in size of the chest cavity and of the compressed lung and in which there is also slight left hypertrophy. They are rarely due to primary sclerosis of the pulmonary artery, but Sanders, Hart, Krutzch (lit.) point out that even the smallest branches of the pulmonary artery must be taken into consideration (see also Schutte).

Not rarely, there is a secondary "wearing out" sclerosis under the conditions named, which causes circulatory difficulty and pressure increases in the pulmonary artery (see W. Fischer).

If no hypertrophy develops in spite of obstruction in the lung, as we frequently find in phthisics, although not always (Reuter, Wideroe), because in chronic cases it does become hypertrophic, it is perhaps due to insufficient nutrition of the muscle or to the decrease in the quantity of blood so frequently observed in pulmonary tuberculosis and consequently the work of the heart is not increased. The dilatation is often considerable, (for hypertrophy in pertussis, see Brick).

(*b*) Causes of hypertrophy and dilatation of the left heart are valvular lesions chiefly of the aorta; arterio-sclerosis, as a cause, is inconstant, (see Marchand). Distension of the aorta is responsible for some degree of cardiac changes, (Wideroe). They occur in aneurysms of the ascending aorta, if they open wider the aortic ostium (see p. 42), or if the valves are sclerotic (see Lehmacher). They develop in chronic renal diseases, especially in the true arterio-sclerotic contracted kidney which is particularly combined with hypertony, even in the earliest stages, when the disease is recognizable only microscopically. They are present also in the nephritis of measles and of scarlet fever after several weeks duration in which the right ventricle also becomes hypertrophic, although to lesser degree.

(According to Wiesel, Aubertin, and Clunet, left cardiac hypertrophy occurs in medullary hyperplasia of the adrenals.)

(*c*) Hypertrophy in both halves of the heart or a small section of them; besides valvular lesions there are tissue changes of the myocardium (fatty degeneration, scars in the muscle), pericardial synechiae, adhesions of the pericardium and the mediastinal connective tissue, chronic renal diseases (see above), from chronic pressure to the ureters with subsequent hydronephrosis; (see above), kyphoscoliosis as causes of hypertrophy. In the so-called idiopathic cardiac diseases, there are dilatation and hypertrophy of the cavities and walls without valvular lesions, or impeded circulation from a pulmonary, renal, (requires microscopic investigation), or vascular disease. We doubt the existence of a purely idiopathic cardiac hypertrophy.

Hypertrophy is physiological if it develops as an adjustment to increased labor (in heavy labor and certain sports), and according to Krehl-Hirsch, it is only a proportional increase in the weight of the heart corresponding to the increase in the bodily musculature. It develops without difficulties or symptoms; when the latter appear, it becomes pathological. This so-called idiopathic dilatation and hypertrophy is seen sometimes in persons occupied with very hard work (laborer's heart)

especially when free, deep, breathing is impeded (boatmen, porters, packers, mine-workers, etc.) and when also, to use an expression of Seitz, an excessive task is demanded of the heart. The hypertrophy in these cases may be enormous, (bucardia); Baumlein saw a heart weighing 540 gms. in a 31 year old acrobat (see also Hasebroek). The so-called Tubingen heart (Munzinger) of the hard working vintners of Tubingen, belongs to this class.

In other cases, there are anemia, chlorosis, or previous severe diseases (typhoid, diphtheria, see p. 61) causing weakness of the myocardium which leads to acute dilatation from but moderate over-exertion without preceding hypertrophy. The heart may readjust itself during rest, but eventually will cause death, perhaps suddenly. This may occur with assumed healthy hearts after forced marching, mountain excursions, sport activities, bicycle riding, etc.

In plethora, which, among other causes, is sometimes due to excessive beer drinking, there not infrequently develop hypertrophy and dilatation in individuals, who, at the same time, are doing hard physical labor, (Munich beer heart); in the majority of cases, there are no anatomical changes in the heart muscle. The physical action of large quantities of fluid which are added indirectly to the blood, the toxic action of the alcohol, (see also v. Otto), and the nutrient qualities of beer must all be considered (Bollinger), a conception which, however, often encounters skepticism from the clinical side, (lit. by Thorel). Arterio-sclerosis and kidney contraction are thought of as contributing factors, (see, *e.g.*, Kraus, Hecht). Moenckeberg classes the "beer heart" as well as the Tubingen heart among the cardiac hypertrophies caused by hypertony; the kidneys, he says, without necessarily having developed to the picture of contraction, nevertheless show arterio-sclerosis. But only numerous observations will enable us to answer all these questions with any certainty. Other cases are considered due to abuse of spirits in other forms, to nicotine, coffee, or even nervous influences. Purely psychic influences on heart action (see Tendeloo) are also held responsible for hypertrophy, but, on the other hand, they may also explain severe diminution of the working capacity of the heart.

Cardiac hypertrophies occur with goiter as partly mechanical from impeded respiration and partly thyreotoxic as in Basedow's disease where there is also increase in blood pressure, (caused by excess adrenalin in the blood?, see Minnick, His, Kraus, Scholz). See under thyroid gland.

### Changes in the Shape of the Heart in Hypertrophy and Dilatation

In ventricular hypertrophy, the trabeculae become rounded, project, the recesses are deep, the papillary muscles are thick and appear shorter.

In auricular hypertrophy, the pectinate muscles become conspicuous as prominent combs (fig. 30).

In ventricular dilatation, the trabeculae are flattened, the papillary muscles narrow, thinned and pulled out lengthwise.

In hypertrophy of the right ventricle, the external appearance of the heart changes so that the right ventricle is turned toward the left, and in observing the heart in situ, the left ventricle and especially its auricle become more or less invisible. In high degrees, the right ventricle alone is the apex situated lower than normal. The heart has essentially increased in width, chiefly at the base, it becomes plump, more nearly square, relatively shortened, the apex is broad, the corners rounded and perpendicular to the midline.

If hypertrophy of the left ventricle predominates, the apex of the heart is formed practically by the left ventricle, and is displaced to the left. The papillary muscles "ride" upward, the intrapapillary space is enlarged (details by Kirch). The heart becomes long, cylindrical or conical in shape. If the right ventricle which appears like an appendix of the left is opened, it looks flattened because the ventricular septum bulges into it, (cross sections through the heart like fig. 20, are very instructive). In pronounced dilatation of the left ventricle, *e.g.*, in aortic insufficiency, the apex broadens (fig. 13), becomes spherical, and gives the ventricle the appearance of a pumpkin, (details by Kirch).

In reference to cardiac hypertrophy with experimental aortic insufficiency, see Stewart, lit.

In general hypertrophy and dilatation (so-called total cardiac aneurysm) the heart becomes spherical and so large that comparison with a bullock's heart is justified (cor bovinum, bucardia); its weight may be four times the normal and more.

Quite extreme enlargement occurs in congenital lesions, especially defects of the septum (persistent foramen ovale). Herzog saw a heart the size of 5 fists in a 22 year old girl, and in a case of Sternberg, the heart of a 16 year old boy had a cross circumference of 46 centimeters. Hypertrophic hearts repose at a lower level with their apex to the left, and, as a whole, across the diaphragm, causing displacement of both diaphragm and lungs.

### Thrombus Formation in the Heart

(APPENDIX. POST MORTEM CLOTS)

We have previously stated that thrombi form in the heart, as in endocarditis, in which the materials are precipitated on the altered valves, *e.g.*, valves showing fatty degeneration (valve thrombi). They also occur in various places in which the walls (endothelium or muscle), have undergone

changes in some manner, as ulcerations and aneurysms (parietal thrombi). We see them in trauma,. *e.g.*, where a surgeon placed a suture, but thrombosis may not occur at all in either the heart or the valves. There is a special kind of parietal thrombus, the so-called cardiac polyps, which are differentiated from other thrombi by their globular or polypoid form. These are found in the ventricles between the trabeculae, mostly toward the apex, (fig. 31), more frequently in the right than in the left ventricle (hypertrophic, and then fatty degenerated and dilated) as well as in the dilated auricular appendages.

They begin as white thrombi (platelets-leucocytes-fibrin) within the recesses between the trabeculae and grow in layers upward as new masses from the blood are continually deposited, (ribbed arrangement). Their

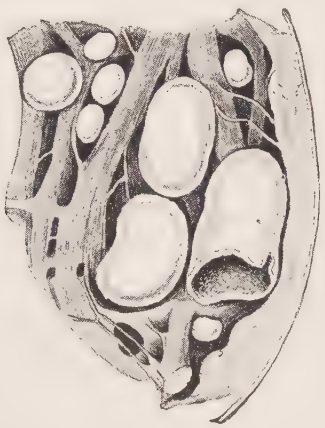


Fig. 31.—Globular and spherical parietal thrombi between the trabeculae of the markedly dilated right heart. To the right a centrally softened thrombus with contents washed out; nat. size.

upper surfaces become rounded, usually hemispherically, (especially in the ventricles); they are usually smooth, but sometimes delicately ribbed, especially in the auricles, and they project like buttons (boutons du coeur) into the cardiac cavity. They may grow to the size of a walnut. Thrombi which form in the auricular appendages between the pectinate muscles soon protrude like polyps into the auricle almost completely filling it. They are arranged in layers, or are more uniformly mixed, with ribbed or smooth surfaces (figs. 32 and 33).

Button-like thrombi may undergo decomposition, soften by autolysis, and then contain a creamy yellowish, or white, or chocolate colored mass; they may break or tear open, evacuate, and leave cavities the size of a bean; embolism may follow. The ancients called these softened thrombi, "pus bags," on account of the puriform appearance of the contents.

Organization is rare, and chiefly in the left auricle; the thrombi become hard and white like fibromas for which they may be mistaken, (see Bostroem, Oppenheimer, and chapt. V). Parietal endocardial fibrosis may be due to organization of flat parietal thrombi (see p. 38).

As causative factors of these thrombi must be considered:

(*a*) Dilatation and congestion as caused by cardiac lesions.

(*b*) Pathological changes in the myocardium, acute or chronic, which make forceful systolic evacuation impossible so that the parietal blood current is delayed and eddies are produced in the deep recesses which cannot empty completely of blood (see v. Recklinghausen).

FIG. 32.—Ribbed thrombus in left auricle; 34 year old woman with mitral stenosis; $\frac{3}{4}$ natural size.

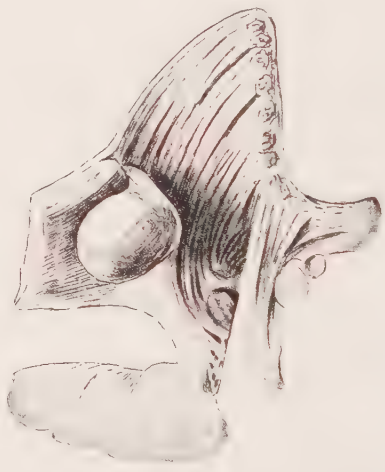


FIG. 33.—Pedunculated thrombus, polypoid with smooth surface in right auricle; 45 year old man with mitral insufficiency; chronic nephritis.

(*c*) Local, often only slight, changes in the wall, such as fatty degeneration of the endothelium may be responsible.

Occasionally, there is found a rounded, freely movable thrombus, the so-called "ball thrombus" in the left auricle, rarely in the right, usually in stenosis of the tricuspid valve, (W. Wood, v. Recklinghausen). It is formed from a detached thrombus, especially of the left auricular appendage, and enlarges and becomes rounded from rolling and turning in the blood stream. This term does not include every kind of thrombus but only the spherical free thrombi. In a case at Breslau (32 year old woman), on removal of the heart, a perfectly round grayish red thrombus rolling like a ball, fell out of the left auricle; it had the consistency of a soft rubber ball and was 3 centimeters in diameter, one-half of its surface was smooth while the other half showed a filigree of pillars and dots. It

had caused none of the symptoms described by v. Ziemssen, for although the mitral ostium had an opening barely the size of a lentil, the thrombus did not fit closely enough to act as a ball valve. Similar conditions were present in a preparation in the Gottingen collection, which P. Stange described as a ball thrombus nearly as large as a hen's egg removed from the left auricle of a man of 21 with mitral stenosis.

### Differentiation between Thrombi and Post Mortem Coagula

Thrombi formed during life are solid deposits from the blood and are differentiated from blood coagula formed after death by these points: (*a*) blood coagula are lumpy, loose, soft, uniformly dark red masses lying loose on the cardiac wall and entering trabeculae but slightly, they are composed of fibrin threads containing red and white blood cells; if the blood clot contracts, the serum is forced out. The blood coagulates quickly before the red blood cells have time to settle or before the plasma can separate; if the latter coagulates, however, it resembles "bacon rind." (*b*) "Bacon rind" or fibrin coagula depending on the density of the fibrin mass are elastic, loosely or tightly meshed with long threads; depending on the serum content, moist, dry, soft, jelly-like, or tough; and according to the number of platelets and leucocytes between the fibrin masses and on the lower side of the "bacon rind," homogeneous, yellowish white or yellow. They are often branching and enmeshed between the trabeculae, apparently adherent, but can be freed entirely. Coagulation is slower. The red blood corpuscles settle, the clot and plasma separate, and the latter coagulates, thus forming the "bacon rind." Frequently (*a*) and (*b*) occur together, side by side, or one above the other, or admixed. In the dorsal position of the cadaver, the bacon rind is above (see Marchand).

If the agonal period is prolonged, the blood of the cadaver contains more abundant fibrin coagula, especially in the heart, provided there were sufficient fibrin-forming factors. The clotting of fibrin predominates in the dark fluid blood of carbonic acid excess (in death by asphyxia) and, according to Tendeloo, in sudden death as well.

Thrombi are usually dry, friable, tear easily, have no elasticity, while coagula are soft, moist and elastic; thrombi are red, cloudy gray, white, brown or yellowish, often showing their elements irregularly mixed or built up in strata while clots are homogeneous. The surface in contact with the active blood current, (precipitation thrombi), is finely granular, ribbed or shows net-like markings; it is practically never smooth and shiny like that of most coagula; the thrombi are completely or partially attached at their bases while coagula are never adherent, and are only entangled between the trabeculae and chordae.

(See also the interesting dissertations on the differential diagnosis of thrombi and coagula in cadavers, by Rost, Ribbert, Beneke, Marchand, Thorel, lit.)

### Infectious Granulomas

(*a*) Tuberculosis is fairly common, usually secondary to tuberculous pericarditis, and involves the upper layers of the myocardium. (*b*) In general miliary tuberculosis, endocardial, and especially subendocardial tubercles are not infrequently found, with miliary nodules isolated or in groups deep within the myocardium. (*c*) Otherwise, larger tumor-like myocardial tubercles are found ranging from the size of a lentil to that of a goose egg; confluent tubercles are rare. They locate in the ventricular and auricular walls and sometimes directly in the auricular appendages. They may be very large, especially in the auricle. Thus the author described a conglomerate tubercle the size of a goose egg in the right auricular wall of a 70 year old woman (see also Kach). The pericardial surfaces are usually adherent if only partially. In the ventricular wall, the tubercles may be recognized only on cross section, (differential diagnosis of syphiloma, demonstration of tubercle bacilli!). A caseous tuberculosis of the mediastinal nodes is usually the starting point. Hematogenous infection is rarer. General miliary tuberculosis may develop if softened nodules in the myocardium rupture into the heart chambers (see p. 36 in reference to valvular tuberculosis; lit. on tuberculosis of the myocardium by Raviart, McKeand and McKinlay Reid, Binder, Maresch).

**Syphilis,** (see lit. in appendix).—Gummata are rare in acquired lues. They form nodules in various parts of the myocardium, having their beginning in connective tissue; they are soft, gelatinous, caseous, or firmer, if caseous-fibrous, and are usually of the size of a cherry pit to a bean but sometimes as large as a billiard ball. They are often embedded like tumors with perhaps a preference for the septum and left ventricle. They may partially or completely heal by cicatrization; in the latter case, they show firm, pale, yellow, circumscribed caseous gummatous etchings like a map; even old foci may contain muscle fibres, histologically recognizable. Giant cells of myogenous derivation may be quite plentiful (regeneration processes, according to Busse and Heller), and thus the luetic process may be mistaken for tuberculosis; when spirochaetae cannot be demonstrated, an absolute histological diagnosis is impossible as a rule. Scars may calcify. In a case of Vaques and Esmein with Stokes-Adams syndrome (periodic bradycardia with fainting attacks), a sclerogummatous focus was found in the bundle of His (see p. 20). Extension of a gummatous pericarditis is rare. Syphilitic newborns show diffuse interstitial myocarditis, and multiple small gummata; larger ones are

comparatively rare. Spirochaetae have been found. For actinomycosis, see under pericardium, lit., (Thevenot).

In leukemia, small and sometimes large nodules are occasionally seen, also in myeloid chloroma (Micremet). At times there are excessive leukemic infiltrations of the heart muscle which make the walls thick and give them a glassy appearance. The grayish red and larger dull light gray areas show microscopically a thick infiltration of cells like a malignant tumor. The endocardium and valves may also be involved (see Reim).

In mycosis fungoides, infiltration of the heart muscle was seen by Paltauf and Scherber (see under skin). Schlagenhauser saw intermuscular cell proliferation in lymphogranulomatosis (see under lymph nodes).

### Tumors of the Heart

Primary tumors are very rare, and usually an accidental finding; some are congenital; (see p. 80, organized thrombi must not be mistaken for tumors). There have been reported, fibromas, hemangiomas, and, externally similar to the latter, varicose-cavernous formations, (Weber, Escher, lit., Schuster); lymphangiomas (Escher); lymphangio-endotheliomas, (Armstrong and Monckeberg); lipomas, (Dittrich, lit.); leiomyomas, (Justi); sarcomas, (Assurini, Crescenzi, Sternberg, Binder, Tobiesen, lit., Meroz, lit.). [Primary spindle cell sarcoma reported by Beck, C. S. and Thatcher, H. S., Arch. Int. Med., 36, 830, 1925.—*Translator.*] Myxomas are apparently more common, and have been called hemangio- or fibromyxo-elastomas, (see de Vecchi, lit., Brenner, lit., Meroz, lit.); they appear mostly in the left auricle, but the author saw one filling the right auricle with a hemispherical smooth mass dipping into the tricuspid opening. They are lobulated, fringed, cauliflower-like, or smooth and globular, glassy, and moist; many are probably edematous fibromas (Jaffe). They may be mistaken for thrombi (see Hiess, Winkler, Stahr, lit., Jellinek). Most of the myxomas described on the valves are probably not true tumors (see Koechlin, and in opposition Hanser, lit., Bergstrand, lit., Staffel). Rhabdomyomas, (v. Recklinghausen, Cesaris-Demel, Seiffert, lit.) occur scattered generally throughout the wall, as multiple tumors, reaching the size of walnuts; most of them are smaller, even of microscopic size. They contain glycogen and sometimes fatty tissue, and may be prominent externally or below the endocardium. The cells of cross striated myomas often show multiple nuclei; they are many-branched, spidery, or spindly, and have a distant similarity to ganglion cells. These tumors must be considered embryonal tissue malformations and are frequently combined with tubercular cerebral sclerosis (50% of cases, according to Cagnetto, and Rehder says 63.6%), as well as with multiple tumors

of the kidney, (W. Fischer) which also belong to embryonal tissue misplacements. They occur in young children. The author saw a 3 year old child with multiple rhabdomyomas of the heart and tuberous cerebral sclerosis (see illustr. under brain), and a 7 year old boy who had innumerable coincident renal tumors. Wolbach (lit.) saw a 10 months old girl with multiple rhabdomyomas of the heart combined with multiple nests of glia cells in the spinal meninges; Bundschuh saw tumors of the heart, kidneys, cerebral sclerosis and meningeal tumors; Amersbach and Handorn, on the other hand, described a solitary rhabdomyoma of the heart without developmental anomalies in other organs (lit. in appendix). Sarcomas are metastatic, especially those of the melanotic variety, and are relatively more common than carcinomas (Blumensohn, lit., Offergeld).

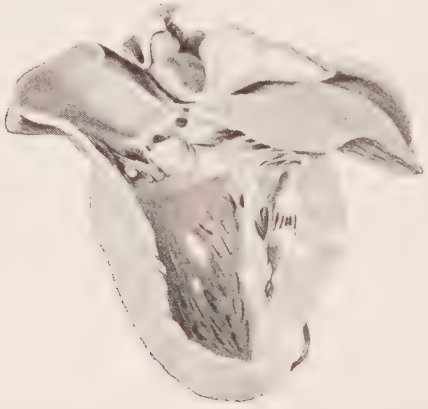


Fig. 34.—Multiple rhabdomyomas of the heart; opened l. ventricle; 7 months old child (Seiffert, Verh. d. deutsch. path. Ges. III day-1901-p. 64-Berlin, George Reimer).

They reach the heart as emboli from a distant tumor focus or by continuity from one in the vicinity, or they invade a vein and thus reach the myocardium or the chambers, especially the right. B. Breus described a testicular tumor (teratomatous), comparable to a hydatidiform mole which grew within the venous system and into the right heart (see also Schmeel, lit.). Kirschner saw secondary hypernephromata.

When larger tumor fragments reach the heart by way of the vena cava, especially if sarcomatous and chondromatous, (a case of Birch-Hirschfeld with enchondroma of the thigh), they occasionally lodge in the tricuspid valve or are attached somewhere within the right heart. The author saw a carcinoma nodule the size of a cherry pit in the right auricle where it had been caught by the trabeculae. This 47 year old man had gastric carcinoma with extension into the thoracic duct. These circumstances are much rarer in the left heart. The author observed a case of sarcoma of

the thyroid, (woman, 56 years old, Basle, p. 293, '03) in which metastases in the lungs were the first stages after breaking through the alveoli of the thyroid. From here, there was an invasion of the pulmonary veins which were filled with long thick cylindrical and fine thread-like tumor masses. A prong the size of a little finger with a long rosary-like thread attached, reached from the right pulmonary artery into the left auricle, while a long knotted entangled thread had caught in the anterior mitral valve leaflet and become partly implanted. The foramen ovale was closed. Metastases to the left kidney were found breaking through into the renal vein (see other cases of tumor thrombosis, lit. in appendix).

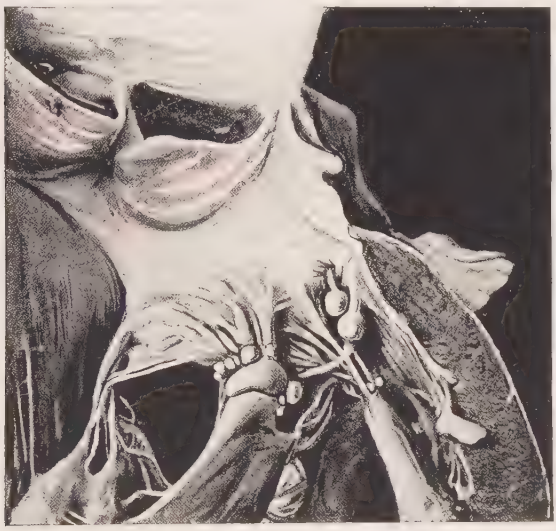


FIG. 35.—Thread-like nodular sarcoma masses caught and implanted in the mitral valve; details in text.

Tumors of the wall may proliferate into the heart and may release secondary emboli. They may also grow through the walls and cause pericarditis, and in rare cases rupture of the heart by softening. As a rule they produce no symptoms.

In melanotic sarcoma the heart muscle may be invaded by innumerable black or spotted, sometimes white, tumor nodules of varying sizes; nodules may bulge under the endocardium, and lie scattered over the epicardium. Sudden death may occur.

Lymphosarcomas and common mediastinal sarcomas (thymus) may invade the heart. In the former case the author saw the left ventricle in a 19 year old man infiltrated to 3 centimeters in thickness.

## Parasites and Foreign Bodies in the Heart

TRAUMA

Cysticerci, which at times occur in numbers, are rare, and not important.

Echinococci are also rare, and mostly in conjunction with ecchinococcus liver. They locate by preference in the septum, and may reach the size of a fist. They may be multiple and open inwards causing evacuated cysts to be carried off as emboli, or they may cause cardiac rupture (lit. by Thorel, Pepere).

As to foreign bodies in the heart (bullets, shot, needles, etc.), which reach the heart directly or after wandering, see lit. by G. Fischer, Loison, Schwarzwald. As to trauma to the epicardium and heart, see pp. 4, 16, 42, 56, also Merkel.

## Malformations of the Heart (and the Large Vessels)

(LIT. IN APPENDIX)

To understand congenital anomalies, the developmental processes of the heart must be touched upon, if only hastily. We recommend, for reference, the works of His, Born, and the text books of embryology by Hertwig and Kolliker, O. Schulze and especially those by J. Kollmann and Tandler. Bencke discusses an interesting conception of the mechanism of development in his article: "Formation and Malformation of the Heart as Functions of Primary Forms of the Blood Stream."

The earliest embryonic rudiments of the heart consist of paired anlage, the two heart furrows, which form from the visceral layer of the mesoderm on each side of the ventral wall, in the area where the upper part of the foregut is later formed; by the time the embryo has reached the length of 2 millimeters, these have combined into the unpaired cardiac tube. At the beginning, the latter consists of two tubes separated by an intervening space, *i.e.*, an inner endothelial tube which lies within the outer muscular tube.

At first, this tube assumes the form of an S (viewed laterally), the venous end (auricular portion) of the S situated more dorsally, while the arterial curved part (ventricular loop) lies more ventrally. The boundary between the auricular portion and ventricular loop is marked by a circular constriction (auricular canal where later the atrioventricular valve forms). It is situated approximately at the transition between the upper and middle third of the middle part of the S. The ventricular loop consists of a descending (left) venous arm and an ascending (right) arm which passes

into the bulbus s. conus s. truncus arteriosus, as a small bulging, and finally into the aorta (fig. 36).

The unpaired auricular portion in an embryo of 5 mm. length, already shows two large sacculations, the two auricles which enclose with their free edge, soon indented, the truncus arteriosus and a portion of the chamber surface from behind. Later the auricular canal receives the

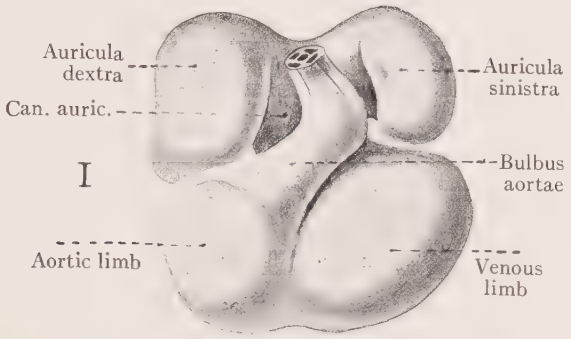



Fig. 36.

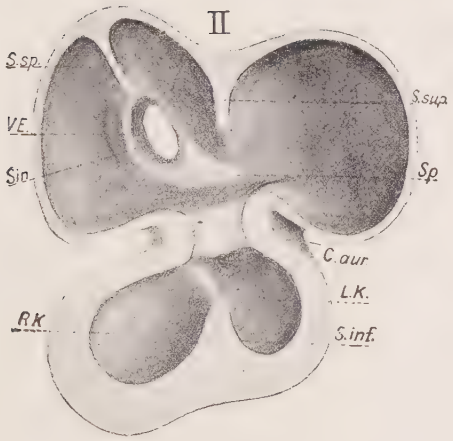



Fig. 37.

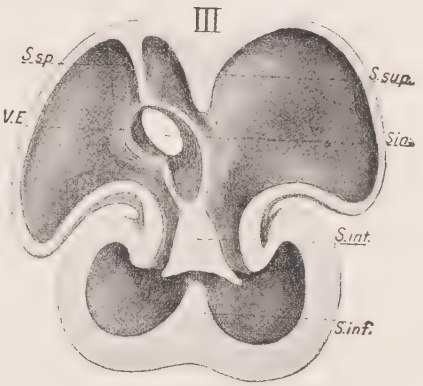



Fig. 38.

Figs. 36–38.—I. Heart of a human embryo 5 mm. in length, anterior view; × 30; according to His. II. Dorsal half of heart of human embryo 10 mm. long; halved in frontal direction; inner view. According to His. III. Dorsal half of a heart divided as II. Embryo 5 weeks old; according to His. S. sp., spurious septum; V.E. Eustachian valve; Sin. mouth of the sinus reuniens; R.K. right ventricle; L.K. left ventricle; S. sup., superior septum; S. inf., inferior septum; S. int., intermediate septum; C. aur., auricular canal.

sinus venosus from behind (sinus reuniens, His), a short wide vessel which receives all veins (yolk, umbilical and body veins).

The septum which divides the chambers and the bulbus arteriosus into a right and left half, is arranged as illustrated in figs. 36 to 38.

**Formation of the Auricles.**—From the upper wall of the unpaired auricle, a shelf descends (septum superius, septum primum, Born),

(fig. 37), which gradually grows into a crescent-shaped plate touching the anterior and posterior auricular walls until it unites with the thickening in the auricular canal which is called the endocardial cushion or bud. The endocardial buds on the right, alongside the superior septum, now grow upward in a sickle-shaped fashion on the anterior and posterior wall (septum intermedium, His) and cooperate in the formation of the auricular septum by uniting with the septum spurium (septum II, Born) which develops quite close to the right of the septum superior. Thus we have a double septum of the auricles. During the downgrowth of the superior septum and at its place of insertion, there is formed secondarily a rounded defect, the foramen ovale, which soon receives a wall or frame from the sickle-shaped extensions of the endocardial bud and the septum spurium, (Limbus Vieussenii). The valve of the foramen ovale situated on the side facing the auricle is furnished by the septum superior. The valve to the left of the opening of the sinus venosus blends with the posterior edges of the foramen ovale. The right valve of the sinus venosus remains isolated, and shares in the separation of the sinus venosus to form the Eustachian valve of the inferior vena cava, and the Thebesian valve of the coronary vein; the membranous valve of the foramen ovale is formed by the left septum superior. Union of this membranous valve with the muscular septum closes the foramen, usually by the end of pregnancy. Fibrous threads and networks (spurious tendineae) which are found sometimes in the right auricle are, according to Chiari, the remnants of the septum spurium and of the right venous valve, more rarely of the left. They are inserted on the one side to the Eustachian and Thebesian valves, on the other side, to Lower's tubercle and the crista terminalis, (see also Looser, Pepere, Thilo, lit.). Thrombi may precipitate between these threads and cause embolism. Spurious tendineae in the left auricle, which originate at the anterior margin of the foramen ovale and end on the auricular surface of the large mitral leaflet, are very rare. They are considered malformations of the auricular septi (lit. by Hosch, see also Aschoff) as are tape-like formations, and still broader septa-like plaques (Borst, Thilo, deVries, lit.). In agreement with Hosch, deVries believes these structures are remnants of the primary septum which had grown too far downward to the left.

Formation of the ventricular septum. A crescent-shaped muscular structure rises from the bottom of the ventricular loop—the inferior septum, later, septum musculare interventriculare; its dorsal part extends to the auricular canal and its ventral section to the truncus arteriosus. In the middle a free concave edge permits communication between the separated ventricles through the interventricular foramen. This opening becomes narrowed posteriorly by prolongations of the septum intermedium, men-

tioned above, and later a membrane supplied by the aortic septum finally closes the communication. The formation of the aortic septum is related to the separation of the aortic conus (the truncus arteriosus communis) in the following manner: two endothelial buds in the latter grow toward each other intertwining and forming a septum (the aortic or trunc. septum) which separates the bulbus into two tubes spirally surrounding each other, the aorta and the pulmonary artery. The septum then dips into the ventricle to unite there with the still free margin of the inferior septum where the endocardial cushion is located. Thus by the same process, the aorta and the pulmonary artery are led into their respective chambers while the membranous interventricular foramen is also closed (pars membranacea septi), thus completing the closure of the ventricular septum.

The formation of the valves. The anlage of the semilunar valves consist of three projecting endothelial buds arising from within (see Beneke in reference to the forces at work).

The beginning of the auriculo-ventricular valves consists of the funnel shaped rim of the auricular canal as it reaches into the ventricle, and two tips springing from the lower edge of the intermediate septum which divides the auricular canal. These parts give rise only to the connective tissue rims; the other parts of the atrio-ventricular valves are formed from the ventricular musculature. The fibres of the muscle tube gradually grow into the space between the muscular and the endothelial tubes (see above), filling it with a spongy muscular network into the depressions of which the endothelial tube bulges (trabeculae carneae and recessus). They assume their final shape with their chordae tendineae and papillary muscles by rearrangement of this network below the semilunars.

Among the congenital anomalies of the heart, the most important are:

### Cardiac Defects of Higher Degree

Complete absence, or a rudimentary "anlage" of the heart is observed in so-called acardia. This rare malformation is always found in unequal, one-ovum twins in a common chorion (gemini monochorii inaequales). One of the twins is well developed, the other shows the malformation which may be (*a*) true acardia or holoacardia, total absence of the heart or (*b*) hemiacardia or acardius anceps, a cardiac rudiment unable to function, or a more or less well formed heart. Circulation is carried on in intrauterine life only by the heart of the well formed twin; the blood reaches the umbilical artery, (usually only one is present), through the anastomoses in the single placenta and from there into the systemic arteries of the acardiac. Its current is therefore centripetal, *i.e.*, in reversed direction; after it has passed through the umbilical vein of the acardiac, and the placental anastomosis, it passes back into the umbilical vein, and into the heart of the

well formed twin which may hypertrophy from extra work, as in a case of B. Wolff.

Frequently there is considerable congestion in the acardiac umbilical vein leading to edematous saturation of the subcutaneous tissue. In acardiacs, the embryo as a whole may be malformed to the highest degree, without head (acardiac acephalic), or amorphous, as observed by the author (J. D. Schwarze). This case was a shapeless mass larger than a fist, egg shaped, covered by skin showing both a buccal and a rectal opening (acardius amorphus). It was expelled after the birth of the mature normal child. Or there may be a more or less incompletely developed head present (acardius acormus). In the hernia cardiac, on the other hand, human shape can be recognized, however deformed. (Lit. by Schatz, Ahlfeld, Hunziker, Schubert, Schwalbe, Birnbaum, Herxheimer, Marchand, Kopanicki, Heift, Streit and Wegelin, lit., Schwarze, lit.)

**Malformations of the Orifices of the Large Vessels.** *A*, **with—and** *B*, **without Defects of the Septa**

*A*. Malformations of the openings of the large vessels depend on disturbances during development of the bulbus arteriosus. In one case, the aortic septum (see p. 89) does not develop and there is a truncus and naturally a corresponding absence of a part of the ventricular septum which otherwise is derived from the aortic septum. The auricular septum may also be absent, and perhaps the portion (its upper part) of the ventricular septum which is derived from the intermediate septum, so that there is a patulous interventricular foramen. If the development of the aortic septum (which begins above and progresses downward) is complete above, but absent below, the aorta and pulmonic spring from one trunk (conus) naturally leaving the ventricular septum open. The auricular septum is, as a rule, developed, usually with a patulous foramen ovale. Faulty direction, *i.e.*, absence of the spiral turn of the aortic septum will reverse the positions of the ostiae (transposition of the large vessels). Then the aorta is on the right and anterior, while the pulmonic, the lumen of which may be narrowed, is displaced to the left and backward. There may, or may not be a defect of the ventricular septum. In such cases venous blood from the right auricle flows into the aorta, while blood from the left auricle, arterialized in the lung, returns to the lung by way of the pulmonary artery. Then we see extreme cyanosis. Life is possible for some time, only when the blood can be mixed, *e.g.*, through a septum defect, or, as the author saw in an 11 year old boy, through two large defects in the ventricular septum, or through an open foramen ovale, or through Botalli's duct. There are asymmetrical formations of the ostiae caused by faulty formation of the aortic septum in which the share of one or the other vessel is too

small (stenosis) or the vessel is obliterated (atresia), (usually of the pulmonary artery). Septum defects may, or may not be present at the same time.

The most important alterations are: (*a*) Stenosis of the pulmonary artery with defect of the septum is the most important congenital heart lesion. It is either inflammatory in its origin (formerly assumed), the result of a fetal endocarditis, or more likely, a consequence of disturbed development of the aortic septum which may be accompanied by endocarditis, thrombosis, etc., (Rokitansky, Monckeberg). Beneke considers fetal endocarditis extremely rare; moreover, we must be very circumspect

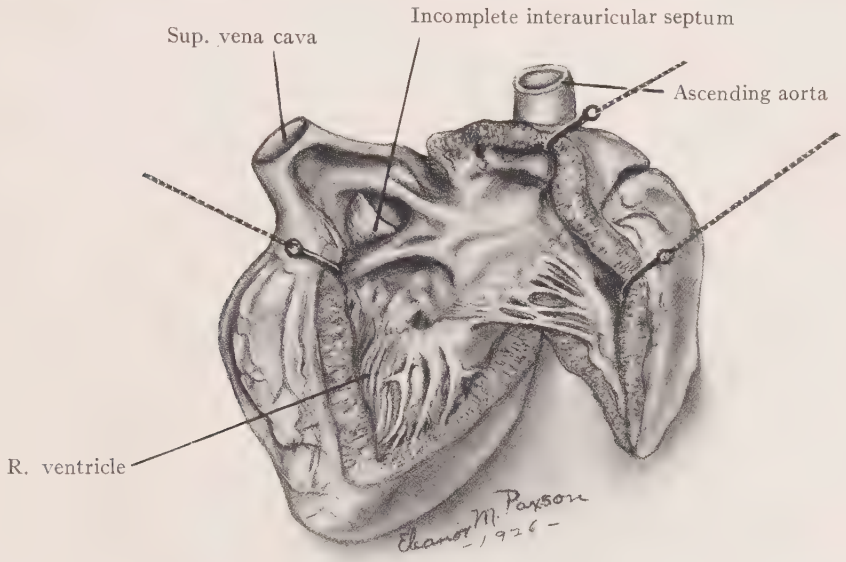



Fig. 39.—Incomplete interauricular septum in child six weeks old, the child, a "blue baby" dying of cardiac failure. L. H. #113.

in assuming the presence of deposits, for sclerotic thickenings of primarily misshapen valves caused by anomalies of the current might easily be mistaken for the results of an endocarditis. Several variations of stenosis occur. Defects of the auricular as well as of the ventricular septum vary in degree, according to the absence of one or the other of their component parts.

**Atresia or Advanced Stenosis of the Pulmonary Artery.**—In place of the pulmonary artery, there is a solid cord or a narrow opening with hard thickened valves which are sometimes fused into a diaphragm with a slight convexity upwards showing a minute hole on its apex. Septum defects are present. The beginning of the aorta rides, so to speak, over the septum, which is displaced toward the left within the area of the defect, and in this way may receive blood from both ventricles (the aorta arises

from both). Both branches of the pulmonary artery are then supplied from the open duct of Botalli. The foramen ovale is open.

**Stenosis of the Conus Pulmonalis.**— Stenosis, muscular at the beginning, later fibrous, occurs mostly in the lower portion, and may be so advanced as to form a narrow slit from which the upper part of the conus can be entered; it may give the impression of a supernumerary ventricle from which the pulmonary artery projects. The right ventricle is markedly hypertrophied and dilated. There is a defect of the ventricular

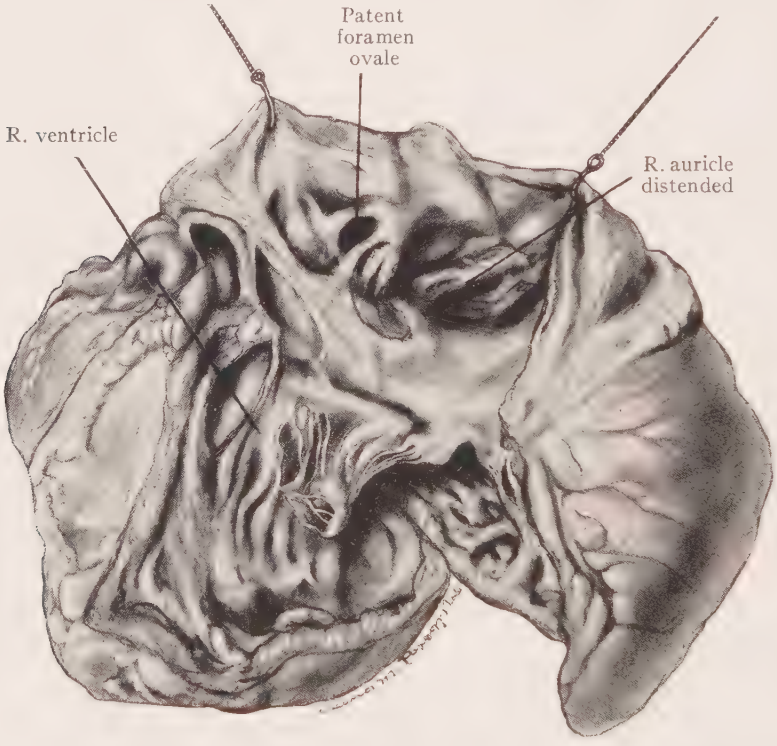



FIG. 40.—Patent foramen ovale in a woman, 45 years old who died of cardiac decompensation. L. H. #118.

septum below the opening of the aorta. Botalli's duct is open or closed. The foramen ovale is mostly open. These may be combined with defect of the auricular septum, transposition of large vessels, *i.e.*, with the aorta displaced to the right and riding on the defect of the septum, and with its origin from both ventricles. There may eventually be stenosis of the aortic and mitral valves and stenosis of the aorta. It depends on the degree of change whether the condition is compatible with life or not. The symptom complex also differs. In moderate stenosis, hypertrophy of the right ventricle may guarantee sufficient circulation for some time. With decompensation, cyanosis appears. In the most

advanced stenoses, a vicarious supply to the pulmonary arteries is furnished by collateral dilatation of the mediastinal, pericardial, and esophageal vessels and especially the bronchial arteries (see for details, Christeller, lit. and Herzog). If the ductus Botalli is open, it naturally carries the greatest amount of the pulmonary blood supply. Individuals with congenital pulmonary stenosis usually die before the end of puberty (see Pommer and Herxheimer). Quite frequently, (according to Vierordt, about 28%) phthisis is the cause of death in pulmonary stenosis, but, according to Burke, it is rather the coincident aortic stenosis which seems to create a predisposition to tuberculous infection. Venous hyperemia of the lungs produces the contrary (see p. 47).

(*b*) Aortic stenosis and atresia with septum defects are uncommon. In such cases, the wide pulmonary artery is connected with both ventricles and continues into the descending aorta. Death usually occurs not later than the twentieth year. Pure aortic stenosis of inflammatory origin without other lesions, is seldom, if ever, found, (Ganeff, Monckeberg, lit. by Thorel).

### *B*. Stenosis and Atresia of the Openings of the Large Vessels, as Well as of the Atrio-ventricular Openings, without Defect of Septum

(*a*) Stenosis and atresia of the pulmonary aorta without defect of the ventricular septum are rare. The tricuspids are usually misshapen and the foramen ovale and Botalli's duct are open. These changes are partly of inflammatory origin and developed only after the septum formation is completed (Sternberg).

(*b*) Stenosis and atresia of the aorta without defect of septum, rarely affects the mouth or the trunk of the aorta, but when found, the left ventricle as a rule is narrow (the author observed one barely the size of a lentil with the parietal endocardium much thickened). Foramen ovale is open; Botalli's duct is patulous; conus stenosis may be added. Cause: supposed endocarditis during fetal life (see Herxheimer, in opposition, Beneke) or, according to Dilg, valve reduplication. Individuals with aortic stenosis may live for some time, but atresias lead to death soon after birth on account of the congestion of blood in the lungs and in the left ventricle (lit. Monckeberg and Schroeder).

So-called isthmus stenosis is not so rare. The isthmus of the aorta consists of the area between the left subclavian artery and the mouth of Botalli's duct. Occasionally, but only in the newborn, there may be seen (1) a tubular narrowing, or, chiefly in adults, and more frequently in males of even advanced age, there may be found in an area corresponding to the opening of Botalli's duct or close below it (2) a funnel-shaped

narrowing or a circular stenosis, as if caused by a ligature large enough to permit passage of only a fine probe, or perhaps a saddle-like constriction; there is occasionally total obliteration; atresia may also be found.

If stenosis, as in (1) is marked, the duct of Botalli remains patulous, while in (2) it is naturally obliterated. A crescent-shaped or circular diaphragm may arise within. Obstruction is avoided by collateral tracts between arteries from the subclavian to the body wall, internal mammary, transverse scapular, deep cervical, and branches of the descending aorta, and especially the intercostals; or through the anastomosis between the internal mammary and the inferior epigastric to the iliac artery. The author saw the internal mammary artery dilated to about four times its normal dimension in a 33 year old man. There may be no consequences during life (Vierordt, Bonnet, lit., Strassner). Hypertrophy and dilatation of the left ventricle (see Lommel), or of the entire heart, are not rare; arterio-sclerosis in the aorta in front of the stenosis, thickening of the endocardium of the left ventricle as a whole, and also of the aortic leaflet of the mitral valve (result of blood pressure), are rather frequent. Occasionally, disease of the valves of the aorta develops; there may be but two leaflets, and asymmetrical pulmonic valves may be present at the same time. But there are also cases in which the aorta is smooth, or shows thin walls. Among the most important complications are rupture of the aorta and dissecting aneurysm (see under this heading, other details by Monckeberg, Oberndorfer, Moriani). The explanation of the frequent cases of the adult type (2) which, however, have also been seen in the newborn, is furnished by the conception of an endarteritis arising from the obliterated duct. In the newborn type, there is a developmental disturbance in which a part of the aorta persists as the fetal isthmus, or the isthmus is completely absent (very rare, lit. Kohl), or there is a grave malformation reaching back to an earlier epoch—agnesia (lit. by Herxheimer; see also, Lommel, Verocay, Hart).

Rare instances of cord-like occlusion of the aorta in other places, as in Hasler's case, close above the diaphragm, are not malformations but acquired defects, (thrombosis with organization); the collateral circulation is carried on through the internal mammary and the inferior epigastric arteries which are as big as a finger.

(*c*) Stenosis and atresia of the atrio-ventricular openings may be related to fetal endocarditis (?) or to faulty development which may also be expressed by the irregular formation of trabeculae. In a child 4 months old, 60 cm. in length, the author saw stenosis of the mitral valve and defect of the ventricular septum, with hypertrophy of the right ventricle; the heart weighed 98 gms. This is quite rare, and is usually combined with changes in the arteries.

### Septum Defects with Normal Vessel Openings. Ductus Arteriosus of Botalli

The auricular septum (with closed foramen ovale) may be completely absent or partially defective (see Gellert, lit.). In the first instance, it causes cor triloculare biventriculosum, which may be combined with a narrow aorta and a wide pulmonary artery (lit. Zeidler). Defects of the ventricular septum may be complete; when combined with defects of the auricular septum we see the cor biloculare which has one ventricle and one auricle; or the ventricular septum alone is completely or partially absent as in cor triloculare biatrium.

Individuals with such imperfections usually die within the first few days. Partial defects of the ventricular septum, defects of the whole of the auricular septum, smaller defects of the auricular septum, defects below the opening of the aorta, (Preisz), and the more occasional malformations in the middle of the septum or near the apex are classed as inhibition disturbances. The clinical picture of de Roger's disease corresponds to an uncomplicated open ventricular septum (see H. Muller, lit.). This anomaly continues throughout life, usually without occasioning serious difficulties, but there is a tendency to pulmonary diseases such as pneumonia, and tuberculosis. The gap must be large to cause functional disturbances and cyanosis. Aneurysms of the pars membranacea are quite rare (lit. Hart); they may perforate.

Persistence of the foramen ovale is very frequent, and found in practically one third of all bodies even up to advanced age. There is not an actual defect, but a diagonal slit due to incomplete fusion of the valves. Such cases show no consequences, since the slit is relatively narrow (at most of the thickness of a pencil) and the valve is forced against the septum by the blood pressure and thus closed. But the lumen may become stretched when there is distension of the auricles, and thus become patulous. Perhaps reopening may take place.

A persistent foramen ovale deserves mention because it permits emboli to enter the greater circulation. Fat, (Fromberg), tumor fragments, etc., which enter the right heart through the cava have all been described (crossed or paradox embolism). Occasionally an embolus may be found actually protruding through the foramen. (Illustrations by Verse and lit. by Thorel and Kunkel.)

Non-closure of Botalli's ductus arteriosus (historical critique by Fromberg). This duct passes from the pulmonary artery into the aorta and resembles the latter in structure, collapses as soon as respiration begins, and thereafter is promptly obliterated, (functional obliteration, see Thoma) as a rule, within the first or second week after birth. Beginning in the

middle there is contraction and proliferation of the connective tissue of both the intima and the media especially of the latter, although according to Pfeifer, it is almost exclusively the elastic tissue of the media. Its aortic attachment can be recognized permanently as a scar.

Schridde describes another physiological scar in the thoracic aorta from the obliteration of the right aorta after its union in early embryonic life with the left aorta which alone persists (see Kroemer also).

Under certain circumstances (see above), Botalli's duct may remain open for some time, or permanently, (lit. Sternberg, Fromberg, Baumler). In other cases it is obliterated too early (stenosis of the pulmonary artery). Ulcerative endocarditis frequently involves the open duct (Hart, Sommer). Aneurysms of Botalli's duct have also been observed, but according to Simmonds, they are, for the most part, but aortic aneurysms at the region where the ductus entered the aorta. Thrombosis may occur and emboli may leave (Rauchfuss). There are also abnormalities in the course and the outlet of the duct of Botalli (lit. by Herxheimer and Thorel). According to Alexandrowsky, many cases of congenital dropsy are related to stenosis of Botalli's duct. All other congenital anomalies of the form and position of the heart have but little importance in comparison to the changes discussed. A few may be mentioned: hypoplasia, the heart is too small; in true idiopathic hypertrophy it is too large—in a case of Simmonds in a newborn child, the heart weighed 44 gms., while, according to Thoma, the normal weight at that time is 20.6 gms.; in Hedinger's case, (lit.), in a 15 month's old child it weighed 132 gms.; while according to Vierordt, it should weigh 44–47 gms.; the author saw a heart in an 8 months old boy which actually weighed 142 gms. (see also Herxheimer, Riesenfeld, lit. and lit. in appendix). Ectopy is when the heart is displaced into the abdominal cavity, (ectopia cordis abdominalis); the palate (ectopia cordis cervicalis), to the outside through a defect of the sternum, or thoracic wall, (ectopia cordis pectoralis); all are rare, (lit. Greiffenberg) and may be complicated with other malformations, especially abdominal fissure usually due to amniotic adhesions. Dextrocardia, (in situs viscerum inversus totalis regularis) is quite rare with normal arrangement of the abdominal organs; in true dextrocardia, however, all parts are reversed like a mirror reflection with the apex of the heart pointing to the right (lit. by Lochte and Koller, Schelenz, Nagel, Weinberger).

Cardiac diverticulae are quite rare and consist of finger-like prolongations of the left ventricle, usually in combination with defects of the epicardium (Arnold, lit.).

Occasionally, there are abnormal chordae tendineae (see p. 19), and trabeculae, abnormal course of the papillary muscles (especially the right), fenestration of the leaflets (see p. 22); and anomalies in the number of

the semilunar valves—not enough—when there is often an ulcerative endocarditis (de Vries, lit. and p. 33), or too many (4, even 5), more frequently of the pulmonary valve; more rarely, there are saccular or ampullar aneurysms of the valves (see v. Arx, in the pulmonary). Reduplication of the atrio-ventricular openings is very rare (Thilo, lit.). See also lit. of Herxheimer and Thorel. [For congenital cyanosis and a new method of diagnosis of congenital heart lesions, see Hess, J. H. and Pearce, R. G.; Am. J. Dis. Child, 13, 1, 1917.—*Translator.*]

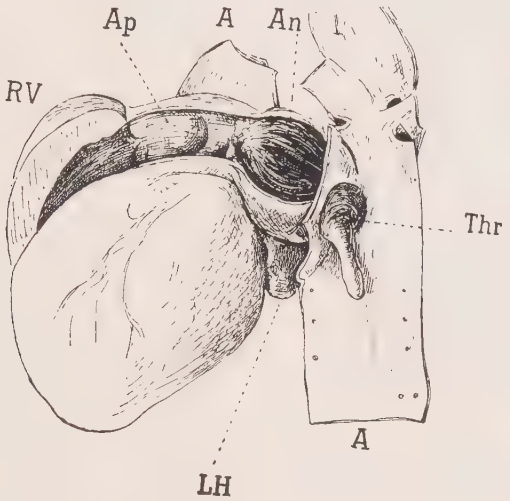



FIG. 41.—Aneurysm of the ductus arteriosus Botalli (An) filled with a thrombus (Thr) which is continued into the aorta (A); R.V., right ventricle; Ap, pulmonary artery; L.H., left auricle, girl 11 days old died of sepsis starting from an umbilical phlebitis.

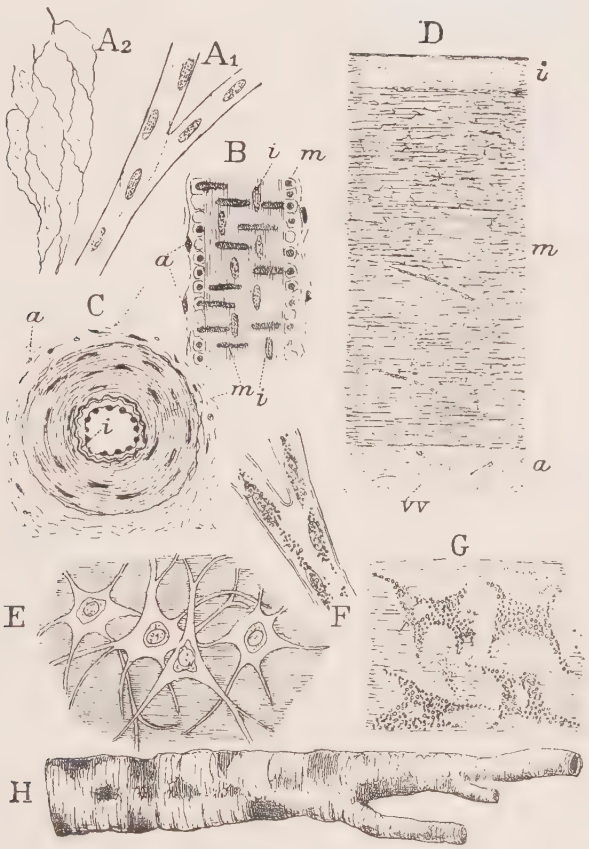
## ARTERIES

**Anatomy of the Blood Vessels.**—The name "artery" arose from the ancient conception that the arteries contained air, because they are empty after death. Veins were called blood vessels, (even today in some languages, *e.g.*, German), while the arteries, in contradistinction, were called pulsating or beating vessels. Arteries conduct blood from the heart, and, with few exceptions, change into capillaries within organs; the capillaries then become veins which return the blood to the heart. Precapillary arteries are called arterioles.

The capillaries are tubules 0.007 to 0.01 mm. in diameter, with walls consisting of a single layer of translucent, long, flat endothelial cells linked together by a thin line of cement substance demonstrable by silver treatment. Each cell has an oval nucleus. The endothelium which forms the capillary wall is but a prolongation of the endothelial tube which lines the

arteries and veins; it allows the exchange of metabolic products between blood and tissues. When the capillaries are abnormally distended, as in inflammation or under the pressure of congestion, fluid and solids of the blood pass through by way of the so-called stomata (Arnold), which probably are only transient gaps of various widths between the delicate, soft, semi-fluid protoplasmic prolongations (intercellular bridges) by which the endothelium is joined together. The capillaries can hold several times the total amount of blood, and are able to contract and expand independent of nervous influences. If the vessels are traced backward to the transition, a fine membrane is found surrounding the endothelial tube consisting of cellular connective tissue—the tunica externa or adventitia. This accompanies the vessel and unites without sharp demarcation with that of the organs and various parts of the body. The tunica media or muscularis lies between the inner and outer layers and first consists of only a single layer of muscle cells. The cells lie parallel, side by side, arranged circularly, bringing their long nuclei perpendicular to the vessel axis, in the direction of which the endothelial nuclei lie. The larger arteries, close to the heart, contain more smooth muscle and elastic fibres; in the peripheral arteries, the media is more robust than the other layers, because they carry the blood through the obstructions offered by surrounding organs (intestines, muscles) with less help from the cardiac systole; in addition they must adjust themselves to circulatory necessities (arteries of intestines, extremities). According to the relative amount of elastic tissue and its fibrillar or coarse character, we differentiate arteries of the elastic, and of the muscular types. (Bonnet; for more details, p. 100). The larger the artery, the more independent is the intima below its endothelial lining and the more complex its architecture. A connective tissue layer intrudes between the endothelial and muscle layer, and contains, among other structures, the so-called stellate intima cells, lying in injectable spaces. These are flat with ovoid nuclei and are scattered in the collagen ground substance among fine elastic fibres, (schematic in fig. E). According to Jores, Voigts, Hallenberger, there is a physiological increase or thickening (hyperplasia) of the intima after birth; elastic fibres are split from the fenestrated, but otherwise homogeneous, inner elastic layer (elastica interna, see below), and small strips of connective tissue with elongated cells are deposited between them. The thickening is considerable in the larger arteries, especially the aorta, and the outer layers superimposed on the elastica interna change by proliferation into an elastic-muscular longitudinal layer (Thoma, Jores), while the inner layer (so-called hyperplastic layer of Jores) is built of strips of elastic fibres. The layer just below the endothelium is of connective tissue. The process by which the elastic ground substance is formed by cells (so-called "elastoblasts")

reaches a maximum, and then remains stationary, (3rd, 4th, 5th decades). Regions subjected to extra mechanical tasks, at bifurcations, etc., show more pronounced thickening of the intima from the very beginning, (adaptation). (For details in relation to the structural modifications in growing arteries, see Thoma, Aschoff, Oppenheim.)




FIGS. 42–50.—$A_1$, capillary; $A_2$, surface view of endothelium; B, small artery cut lengthwise; C, larger artery in cross section; a, adventitia; m, media or muscularis; i, intima; ABC, high power; D, wall of aorta; a, adventitia; V.V., vasa vasorum; m, muscularis in which two vessels pass obliquely; i, intima, bounded toward the media by the elastic lamella, covered within by endothelium (low power). E, so-called stellate cells of the intima, star-shaped spaces with continuations; cells within; × 500. F, brain capillary with fatty degeneration; fat droplets stained black with osmic acid. G, fat infiltration of the intima of the aorta, surface view (high power); H, calcified artery. The chalk rings of the media shine through; normal size.

The internal boundary of the intima is the so-called elastic membrane which on cross section appears pleated and the intima folded from contraction of the muscularis. It has a double outline, is refractile and sharply divides the intima from media; the separation of media from the adventitia by the external elastica is much less sharp.

In medium-size and larger arteries the two elastica are composed of radiating fibres penetrating the media (Durch), so that all the elastic elements are a connected whole. According to Barach, there are more fibres in the arteries of the muscular type. This elastic system is developed for functional reasons. To further resist pressure differences, especially in the large arteries near the heart (the aorta, its main branches, pulmonary artery), the essential parts, *i.e.*, the muscle bundles in the media, cross each other diagonally, and are gripped between elastic layers (Thoma). The elastic fibres are also thicker in the larger vessels (arteries of the elastic type), while the elastica of the media of smaller arteries is arranged in a system of fibrillae surrounding the muscle fibres (arteries of the muscular type). In the smallest peripheral arteries (non-pulsating) the internal elastica resolves into a wide-meshed network of fine longitudinal fibres which gradually end at some distance from the capillaries, (Bonnet, Durck). The number of elastic fibres varies in different regions; it is small in the arteries of the brain (Triepel), but in others it is greater than the musculature (Bonnet). This elastica can be stretched enormously. Ordinary connective tissue is added to the musculature in the media of larger vessels. (See Kani in reference to measurements of elasticity of large arteries.)

Wavy, horizontal, white, tendinous lines on the intima of the aorta, especially its posterior wall, are quite frequent, probably as functional structures (Ernst); they often cross at acute angles and are thickenings of elastic tissue. See Ribbert for their interpretation. The muscularis of veins is less important than that of arteries; the larger veins have an inner elastic layer below the endothelium, but the fibres are also present throughout the wall arranged circularly and almost covering the interrupted circular muscle fibres. Some veins, especially those of the leg (popliteal), have rather a sturdy media; others have no muscularis (pia and dura). The trunks of the portal and renal veins have longitudinal muscular layers throughout almost their entire lengths (Stoehr, Schultzee).

The smaller and medium veins have abundant smooth muscle fibres in the adventitia. (For radiating fibres, see above.)

Larger vessels are nourished by the vasa vasorum passing from the adventitia obliquely through their walls. This includes the intima which is not supplied by blood passing through the vessel. Nerves terminate in the muscle of the media. (See L. R. Muller, Glaser, reinnervation of vessels.)

For microscopic differentiation of blood and lymph vessels—see Glasser.

(In reference to anomalies of large vessels, see lit. by Herxheimer; for congenital stenosis of aorta, see p. 72.)

## Degenerations and Infiltrations of Arteries

### Fatty Degeneration

Fatty degeneration occurs in both the intima and media. The intima shows macroscopic yellowish white spots and striae, usually but slightly projecting, perhaps arranged in the long axis, especially between the intercostal arteries on the posterior wall of the aorta, but occasionally also like a trellis. The intima may be unchanged otherwise.

Microscopically, sections cut in the plane of the spots, show minute fat droplets arranged in a network between the fibrillae and within the spindle and stellate cells of the intima. It should be noted that the change is confined to the superficial layers of the intima and is not in the lower levels, as are the connective tissue thickenings of arteriosclerosis; connective tissue proliferation may be entirely absent (Jores).

It is very common, appearing sometimes in early childhood, or even in sucklings. Opinions are divided as to whether it is a degeneration or an infiltration; Ribbert adheres to the latter view (comp. Stumpf, Hueck). Circulatory disturbances, tension, pulling of the inner layer of the vessel,—according to Stahel the fatty lines within the aorta are pressure lines,—changes in the condition of the blood causing insufficient nourishment of the vessel walls, infections, etc., are held responsible (Faber, Monckeberg, Zinserling); Ribbert excludes infections. Younger, chlorotic individuals (narrow aorta, pressure increase) seem predisposed to these changes, and they are found in the aorta of almost all phthisics. This fatty degeneration is sharply differentiated from arteriosclerosis by Virchow, Orth and many others, but some, including Lubarsch, Jores, Marchand, etc., class it with the latter condition (atherosclerosis), indeed, consider it primary and characteristic. Faber saw all transitions from minute fat spots to atheroma, although he thinks arteriosclerosis starts in the media. Klotz and Manning, on the other hand, are of the opinion that this fatty change which they found so frequently in typhoid fever is an independent process, capable of regression. The author separates it from arteriosclerosis, as do Ribbert, Hueck, Froboese, etc., (see Krisch).

It occurs most frequently in the aorta, carotids, especially at the bifurcations, and the pulmonary artery, especially in congestion from cardiac lesions. On the other hand, the latter is rarely involved in macroscopic arteriosclerosis, although milder degrees of "wearing out" sclerosis are frequent in this artery (see p. 75) as well as in the smaller arteries and capillaries, especially of the brain.

Subsequent to the release of fatty endothelium and superficial lamellae into the blood stream, the shallow losses of substance (fatty erosion, Virchow) may eventually be covered with thrombi.

In a young anemic woman with otherwise unchanged vascular system, the author found a small circumscribed fatty erosion in the ascending aorta on which a parietal thrombus had formed and from which a fatal cerebral embolus had been released. Compare the case mentioned on p. 57 of fatal embolus in the left coronary artery (fig. 51).

The media of the smallest arteries, especially of the brain, also undergoes fatty degeneration; the muscle cells are filled with fat granules; the vessels may tear and cause fatal hemorrhages.

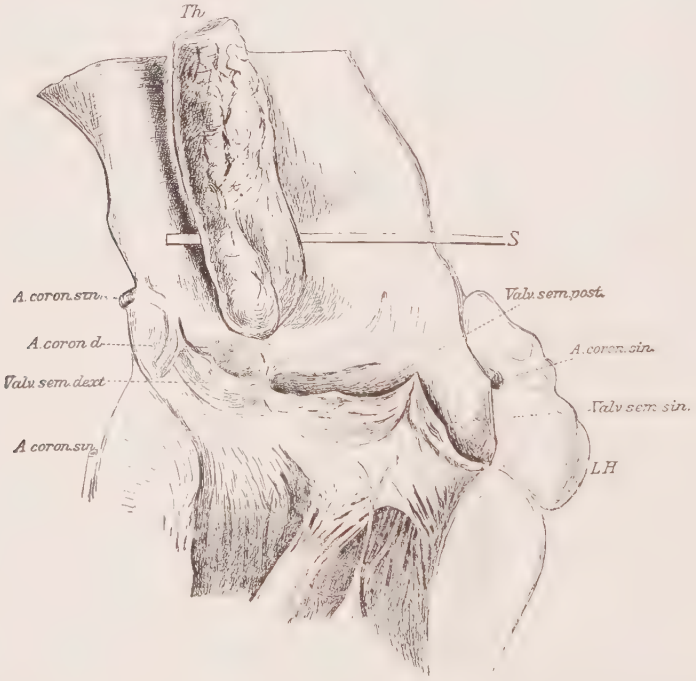



Fig. 51.—Very large parietal thrombus (Th) of the aorta, attached below to (S). The upper portion can be turned over downward. Embolic infarcts in spleen and kidneys. Inner surface of aorta smooth. Cardiac valves intact. L.H., l. auricle; 56 year old man with large carcinoma of stomach; about ½ normal size.

Fatty degeneration of the elastic fibres (Faber), the cement substance (Torhorst), the muscle fibres of the media, or all combined, is found in intoxications, (phosphorus, alcohol), in infections (Faber), in increased pressure (Klotz), etc. It is always present in arteriosclerosis (pp. 107 and forward), especially in regions distinguished by functional thickening of the intima. It may be followed by calcification.

## Calcification

Lime salts are deposited in the cells and fibres, or in the interstitial tissue in the form of small, shining granules or coarser clumps. According

to Klotz, fatty degeneration always precedes calcification which is never found in living cells. According to Hueck, calcification always begins in the ground substance between the fibres.

Reactions of calcium. It dissolves easily in hydrochloric acid with the evolution of carbon dioxide bubbles if the compound is the carbonate, ($CaCO_3$); if the phosphate, ($Ca_3(PO_4)_2$), no gas bubbles are released. The addition of 2% to 3% sulphuric acid forms calcium sulphate with both kinds of lime as crystals of plaster of Paris in fringy, fine, prismatic needles. Place a drop of acid on the edge of the cover glass, lift the cover glass and the drop reaches the preparation; solution of the lime salts and growth of the calcium sulphate needles can be observed. The silver reaction of Kossa demonstrates only calcium phosphate. Place sections for 5 minutes in 1% to 1.5% solution of silver nitrate, wash in water, stain the nuclei. Light reduces the calcium phosphate to black silver phosphate in 30 to 60 minutes. For fatty acid-calcium, see under pancreas. Calcium stains intensively blue with hematoxylin. It occurs in both intima and media, but primarily in the media, in both the elastic fibres and the muscles, particularly in the latter, after preceding fatty and hyalin degeneration with final necrosis. It is primary mainly in the peripheral vessels of the muscular type, especially those of the arms and legs, and is often associated with advanced age, ("wearing out"), plus nutritional disturbances.

Thus calcification of the media of arteries of the muscular type is the expression of arteriosclerosis in its wider sense, although there is occasionally sclerosis of the intima also, especially in advanced age (Monckeberg). In arteries of the elastic type, *e.g.*, the aorta, arteriosclerosis is particularly shown in sclerotic thickening and smeary degeneration of the intima, the so-called arteriosclerosis and atheroma, or in a narrower sense, atherosclerosis. But contrary to the conception of the etiological and pathogenetic unity of arteriosclerosis and calcification of the media of arteries of the extremities (an opinion shared by B. Fischer), Monckeberg separates true calcification of the media from arteriosclerosis for reasons he considers fundamental.

Calcium was found by Ribbert and Faber from the age of 15 upwards in smooth, macroscopically normal, aortas. Lime was found in the pelvic arteries in the first year of life (Faber). All arteries are subject to calcification. Surbek's observation of extensive congenital calcification of the media involving even the smaller branches, is exceedingly rare, and may be explained by assuming there was disturbance of the general calcium metabolism, (calcium gout, M. B. Schmidt). (Appropriate experiments by Katase.)

Chronic diseases such as tuberculosis, the cachexia of tumors, nephritis, etc., influence the amount of calcification. Isolated calcification in

smaller cerebral vessels, both arteries and veins, is often difficult to find; it occurs, but is rare, as is that of capillaries in calcium metastasis (Virchow). Furthermore, calcification as an independent process in older, or, indeed, in quite young individuals, is also rare. Hyalin changes (precipitation of a protein-like "protective colloid," Hueck) seem to precede calcification (Mallory, Hansemann, Eug. Fraenkel, Timaeus). According to Wiedemann (Hueck), the process starts in the adventitial lymph sheaths

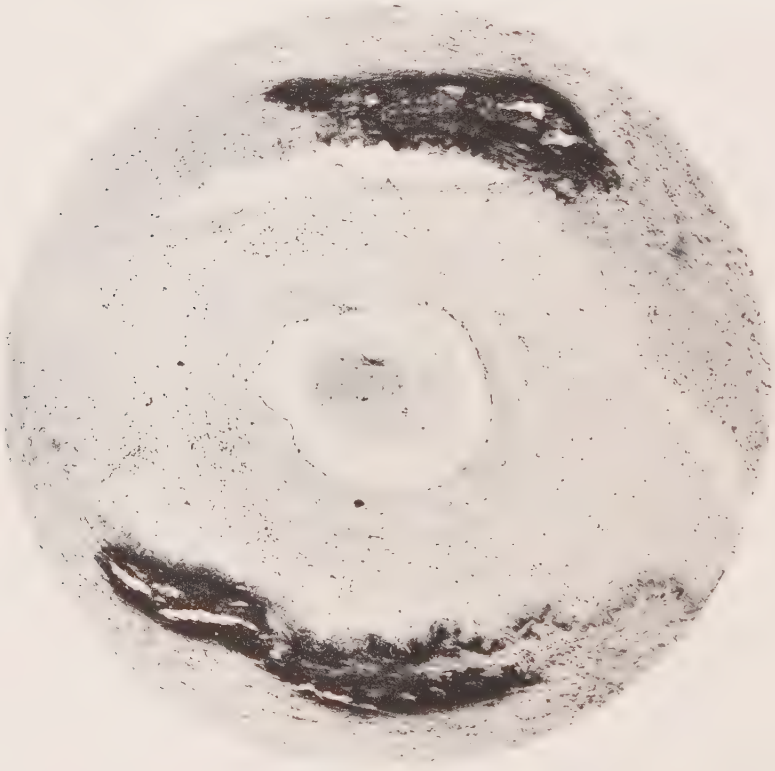


FIG. 52.—Artery taken from above the gangrenous foot in diabetes. Calcification in the media, organization in the intima, and recanalization of the lumen. This is the anatomic basis of most diabetic gangrene. × 70. L. H. #670.

and involves the media later. On sectioning a brain, the calcified vessels may project like bristles and feel hard to the touch. Focal softening can usually be found.

In the arteries of the lower extremities, chalk rings in the vessel walls correspond to the circular course of the media, thus giving the vessel, especially the femoral, a ribbed appearance like a bronchus (goose trachea). The vessel is robbed of its longitudinal elasticity (Hueck). In other cases. the artery becomes a stiff, wavy, fragile, chalk tube. The intima may be

practically unchanged, (Virchow), and no arteriosclerosis at all may be present in internal vessels (Monckeberg). Oberndorfer found that arteries subjected to considerable movement and thus to a kind of massage, such as in the popliteal space, groin, etc., are less subject to clacification than the less mobile and more fixed vessels. Hueck believes the elastic-muscular thickening is related to especially favorable nutritional conditions and is protective against progressive degeneration, fatty degeneration and

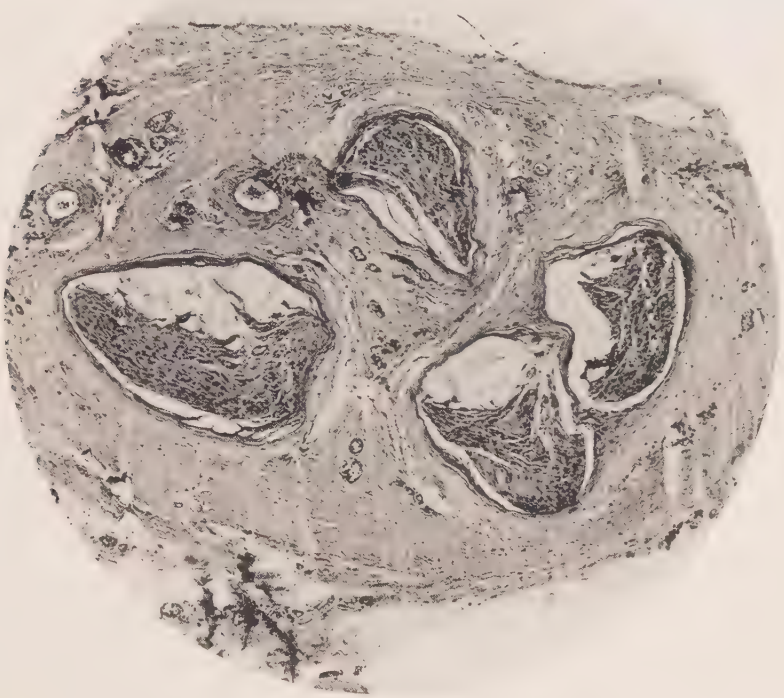


FIG. 53.—Organizing thrombi in veins of the foot; the foot gangrenous for one week. The section taken three or four inches above the gangrenous area. × 120. L. H. #661.

calcification. But the relative frequency of aneurysm in the popliteal artery (p. 109) is contradictory.

Fracture of arteries is described by Klotz in 3 cases of calcification of the media (popliteal and tibialis posticus). Granulation had supplied a form of callus and osteoid tissue was also present. There were no thrombi.

In the uterine arteries, calcification is quite frequent after hyalin degeneration, and, according to Fraenkel, necrosis of the media is very common in advanced age. But there is a hyalin connective tissue change of the vessel walls corresponding to that in the ovaries which is considered a

functional menstrual or pregnancy sclerosis, (Szasz, Schwarz, Pankow, Sohma, Bennecke, Hueck).

Isolated calcification of the elastica interna in arteriosclerosis (Matusewicz-Ernst) is uncommon, but the author has seen it frequently.

Thrombi are readily deposited in calcified arteries, as in the aorta, the femoral and its branches, and even in smaller arteries such as the cerebral, coronary and mesenteric.

Senile and diabetic gangrene are frequent in the lower extremities from thrombotic occlusion of the arterial branches with calcified media and atheromatous intima. (Comp. spontaneous gangrene, p. 120.) In other cases, the gangrene is due to embolism.

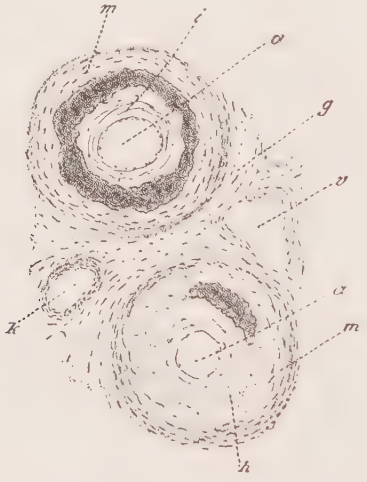



FIG. 54.—Uterine arteries of an old woman; hyalin degeneration and calcification; a, lumen of artery; i, intima; m, muscularis; h, hyalin degeneration; the dark inclusions, (circular in the upper artery) are calcification; K, small arterial branch unchanged; v, small vein; g, fibro-muscular tissue of the uterine wall. Hematoxylin-eosin; calcified areas deep blue (high power).

Metaplastic, true ossification of the vessel wall is infrequent, (Monckeberg, lit.; experimental production, Harvey). It was seen by the author in the carotid, but occurs more often in the aorta, the femorals and their branches, and the uterine arteries. Cartilage is very rare.

### HYALIN DEGENERATION. (Fig. 54)

This is characterized by the thickening and diffuse swelling of a homogeneous, highly refractile mass in the intima (subendothelial layer), and media. These areas tend to calcify. It occurs in both larger and smaller vessels, thus in the media of the uterine arteries (see above), the arterioles of the kidneys, the spleen (media, see Herxheimer), in capillaries, such as in

the glomerular loops, in lymph nodes, and in the brain. The walls of smaller cerebral arteries are frequently thickened while the lumena are narrowed or dilated. (Compare with arteriosclerosis in small arteries of other organs; for rare extensive hyalin in arteries, see Ritter.) Transitions from hyalin to amyloid degeneration are found.

### Amyloid Degeneration

This resembles hyalin degeneration microscopically, but is more lumpy and can be differentiated by its specific reaction. The amyloid, generally localized in the connective tissue apparatus, is always infiltrated and deposited interstitially in the connective tissue. It appears chiefly in the media and intima but not diffusely, so that different regions of a vessel contain swellings; but as the muscle fibres of the media of smaller arteries are crushed, the vessel as a whole, swells and becomes glassy. The connective tissue and elastic fibres disappear in the vicinity. On capillaries, it is deposited as a glassy coating around the endothelial tube, which is narrowed or occluded by the swelling, (glomerular loops of kidneys).

The medium and smaller arteries and the capillaries of the parenchymatous organs of the abdomen, the intestinal mucosa and submucosa, the kidneys and lymph nodes are preferred. Only in pronounced cases of general amyloidosis are the larger arteries involved, and only to minor degrees.

It is a part of general amyloidosis found most frequently, and earliest, under the conditions given in more detail under amyloid degeneration of the liver, (see there for amyloid reaction).

### Arteriosclerosis and Atheroma of Arteries

Arteriosclerosis (Lobstein), the atheromatous process (Forster), endarteritis chronica nodosa s. deformans (Virchow), is a quite common disease causing severe changes in the intima, consisting in part of hard, elastic, hyperplastic thickenings, and in part, of regressive changes in these foci; the other layers participate later, especially the part of the media bordering on the intima. The worst regressive changes are seen in the aorta.

If the conception of arteriosclerosis is interpreted in a wider sense as a progressive nutritional disturbance of the arteries, and if the varying anatomical structure of the arteries is taken into consideration, it is not surprising that there are differences in the pathological pictures. The sclerotic atheromatous process occurs chiefly in arteries of the elastic type, particularly the aorta and the larger arteries leading to the internal organs (heart, brain, spleen, kidneys, lungs).

In arteries of the muscular type (extremities) the changes are more severe in the media (calcification) (p. 104). Sclerosis of the smaller arteries and arterioles (brain, myocardium, spleen, pancreas, liver, kidneys) presents still another picture which consists of thickening of the intima by hyalin degeneration of the connective tissue, hyperplasia of elastic fibres, thickening of the muscularis and adventitia, slight fatty degeneration and perhaps marked calcification of the intima and media. The involvement is not focal but diffuse in the arteries of one or more organs, (see under calcification, p. 103, and hyalin degeneration, p. 106).

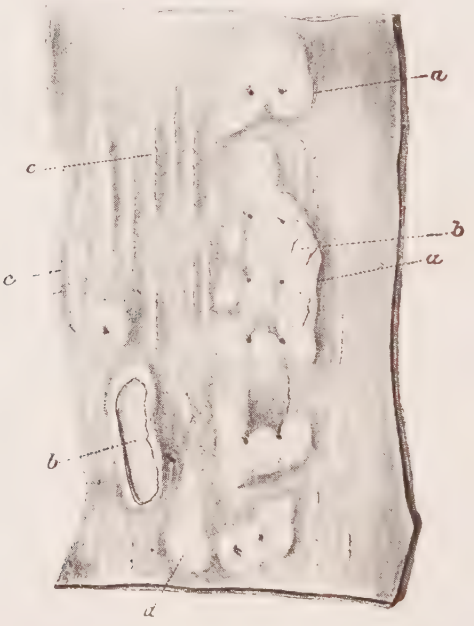



FIG. 55.—Arteriosclerosis of aorta in thorax; a, sclerotic lumps and plates; frequently around the outlets of intercostal arteries; b, smooth calcification plates in the thickened intima; C, fatty degeneration of intima in form of long striae; ¾ nat. size.

If we follow the process in the aorta, we see the first stage as a thickening of the intima by proliferation and swelling; it becomes hard (sclerosis) or calcifies; in the second stage, not always developed very far, there is frank degeneration, fatty metamorphosis, necrosis and softening, (atheroma).

Some vessels are arteriosclerotic without macroscopic softening, and others are softened without much arteriosclerosis, especially in old age. For this reason it is wise to retain the differentiation between sclerosis and atheroma because it helps in macroscopic characterization during autopsy. The author cannot adopt Marchand's designation "atherosclerosis" as derived from the histological picture of the intima, in place of "arterio-

sclerosis." We might reverse it with Orth, and speak of "scleratherosis" since sclerosis is the primary, and softening the secondary change. The consequences are different; embolism is more frequent in atheromatosis, and cardiac hypertrophy is often entirely absent. Pilt, Huchard and Teissier especially, point out the clinical differences between sclerosis (high blood pressure, cardiac hypertrophy, contracted kidneys, etc.) and atheroma interpreted as a disease of senility, (no hypertony). But other clinicians, *e.g.*, Romberg, do not share this conception.

If the different phases of the process are investigated, we see first:

(*a*) Thickening of the intima in plaques, some soft and jelly-like, some fibrous, many hyalin, and some as hard as the cornea or cartilage, bluish white or whitish yellow in color with transitions from soft to hard. The elevations take the form of blisters, cushions or platelets (sclerotic platelets, fig. 55).

In the aorta, the lamellae of the intima are increased in number, the canaliculi are enlarged, the cellular elements proliferate and are infiltrated with fat (doubly refracting), with fatty degeneration in addition, (fig. 56-i). The accumulation of fat is often so abundant that it adds considerably to the thickening. Round cells are found in moderate numbers and in this stage the elastic fibres within the thickened area are, as a rule, increased in number. Other regressive changes soon follow. The old and the newly formed fibrous intima lamellae undergo hyalin degeneration, are swollen, shiny, the striae disappear or are divided here and there by small clefts; finally nuclear staining is impossible. The elastic fibres gradually disappear. These degenerative changes often begin in the depths of the intima.

In the discussion on p. 98, we stated that arteriosclerosis is related to physiological thickening of the intima, according to Jores, Hallenberger and others, in this way: connective tissue develops between the elastic lamellae of the intima thus separating the fibres which become scattered in the connective tissue. Some new formation of elastic fibres takes place coincidently. According to Jores, fatty degeneration of the elastic fibres is the immediate reason or the stimulus for the connective tissue proliferation. But this latter statement was not verified by Torhorst and Hallenberger, who saw thickening with microscopically intact elastic fibres.

Sclerotic plates occur in arteries of various diameters, but most frequently in the aorta, the cerebral, the coronary, and splenic vessels.

The latter are especially exposed to blood pressure effects (systolic expansion and longitudinal stretching) on account of their loose fixation.

The origins of the intercostal arteries from the aorta are especially favored (fig. 55) and annular, stellate, and crescent-shaped thickenings

develop around their narrowed openings. Other favorite places are at bifurcations, *e.g.*, where the carotid divides into the external and internal. Frequently only an occasional vessel or merely a trunk or some branch is diseased; indeed, an astonishing lack of uniformity is often present. There may be severe sclerosis of the aorta and larger vessels with no change in the cerebrals. For this reason, as the author has emphasized for many years, feeling the pulse gives no indication of the general condition of the arterial tree. In other cases, the process is universal. A "hard pulse" may depend on sclerosis or calcification of the intima, but also may be due to the purely muscular and elastic connective tissue hyperplasia of hypertony, as in contracted kidney, lead poisoning, etc., (comp. p. 76). The smaller arteries often show such a marked diffuse thickening of the intima that the media and adventitia appear as a fine membrane from which the thick intima may be pulled out as an inner tube.

(*b*) In the further course of degeneration, the plaques become necrotic, soften and break down. This is called atheromatous disintegration. It is often but slight, and of microscopic extent, but is seen in every pronounced arteriosclerosis. When this change dominates the macroscopic picture, it is called "atheroma" and is typical of so-called senile aortic arteriosclerosis.

On the surface of the plaques or in the deeper layers of the thickened areas, fatty degeneration, necrosis and sometimes mucoid metamorphosis appear. The fatty and necrotic areas are opaque, yellow, fairly hard, and dry at first; later, they become mushy, soft and grumous. The blood stream may wash away the debris and leave erosions, unless disintegration began in the depths, when hardened lamellae appear above, and a cavity forms within the raised area filled with a grayish white, glittering, mushy substance, (atheromatous focus, formerly called, atheromatous abscess). Atheroma debris consists of granular disintegrated tissue, which clears when treated with potassium hydroxide, and fragments of hyalin, fat droplets (reaction for fat, p. 52), and fatty granule globules which are leucocytes loaded with fat. Droplets of a doubly refracting substance occasionally found within foamy, so-called xanthoma cells are cholesterin precipitated in thin plates. The material, colorless after treatment with iodine, stains deeply blue on addition of pure sulphuric acid. In formol preparations, it persists as plates. Lime salts are deposited in the vicinity of the disintegrating focus and in the decomposed tissue.

When the upper layers soften, the atheromatous focus finally ruptures into the lumen of the vessel through a tiny hole; the eddy of the blood then produces an opening with irregular, overhanging edges leading to shiny, whitish yellow, soft material in the crater of this so-called atheromatous ulcer. They are especially frequent in the aorta and its larger branches

and may be covered with massive white or mixed thrombi. Small vessels, such as the coronaries, may be occluded by such thrombi; emboli may be released from larger vessels, but not as frequently as might be expected, even when many ulcers are present. In other cases, the ulcers washed out and made deeper by the inrushing blood stream, initiate a dissecting aneursym. Thrombi are sometimes calcified, at least, in part. Cellular infiltration surrounds the ulcerated area, but the granulation tissue proliferating in the base rarely accomplishes healing. The scars, however, may calcify or ossify, or contract inward with extensions (cicatricial aortitis), so that without microscopical examination, the process is readily mistaken for syphilitic aortitis, (see p. 123).

FIG. 56.—Arteriosclerosis of aorta; i, intima with increased and hyalinized lamellae; finely granular necrosis, fatty degeneration, calcification; a few small vessels within; m, media with two areas of degeneration in which the musculo-elastic elements are destroyed; oblique vasa vasorum; a, adventitia, with vasa vasorum showing thickened intima—unstained—low power.

(*c*) Calcification also takes place in tissue undergoing fatty or hyalin degeneration as in the thickened intima. Thus the hyalin plaques show diffuse calcification, large yellowish white masses, or platelets, or bone-like fragments. True bone formation has also been observed, although rarely. Or the lime is deposited in the intima in small masses like mortar. Ruszn-yak believes the laminated arrangement indicates relations similar to the colloid precipitation and lime deposit in calculi. In fatty degeneration, combinations of fats and calcium salts are manufactured.

As these changes are developing, the larger vessels are deprived of their elasticity, and become so irregular and tortuous that we are justified in speaking of arteriosclerosis deformans, (Virchow, endarteritis).

In later stages as the media participates, the processes are predominantly degenerative, and to a lesser degree reactive-proliferating. There are calcification, fatty degeneration and atrophic destruction of tissue, especially within the innermost layers corresponding to the foci in the intima. In later stages, the muscularis is involved to its deeper layers and bands of chalky connective tissue masses penetrate it, replacing the lost musculo-elastic elements. In earlier stages, isolated foci and branching columns of cellular and inflammatory proliferation surround the vasa vasorum, sometimes in regions corresponding to thickenings of the intima.

The adventitia may be unchanged, or coarsely fibrous. The vasa vasorum (fig. 56-i), especially the veins, are thickened and their lumena narrowed. There is danger of mistaking this for the primary inflammatory diseases of the vasa vasorum so constantly found in early lues, and although Martin and Huchard considered this endarteritis of the vasa vasorum as the primary change leading to arteriosclerosis, it is now generally accepted that these proliferative processes are secondary to degeneration of the intima. Vessels from the adventitia sometimes penetrate the altered intima.

### Nature and Pathogenesis of Arteriosclerosis

The difficult question of the nature of arteriosclerosis has been answered in various ways. Is it an inflammatory or a degenerative process? Does it begin in the intima or media? Virchow's opinion that an inflammatory process of the intima characterizes the disease, (endarteritis, chron. nodosa s. deformans), has but few adherents today, (Orth), and most authors believe with Marchand that it is a primary degeneration of the intima. According to Jores, the sequence is fatty degeneration, (p. 102), thickening of the intima, and atheroma. Marchand, who assumes that the fatty degeneration and atheroma are primary, would have the process called atherosclerosis, instead of arteriosclerosis, (see p. 108).

Thoma believes the start of arteriosclerosis is a non-inflammatory weakening of the intima, which diminishes its elasticity and induces stretching, (angiomalacia or angiomalasic stretching).

The stretching itself may come from functional overexertion, marked physiological fluctuation in blood filling, from acute and chronic disturbances in metabolism such as are induced by gout, scarlet fever, typhoid fever, chronic lead and mercury poisonings, etc. To retain the original caliber, a reparatory, *i.e.*, compensatory proliferation of the intima (angiosclerosis) is necessary; it takes the form of a functional hyperplasia consisting of the development of elastic fibres and connective tissue. Metabolic disturbances lead from angiomalacia (primary stage) to angiosclero-

sis. This entire conception is applied by Thoma in the same way to the veins, phlebomalacia, phlebosclerosis. In time, as the intima remains under constant high tension, and is fibrous, thickened, and hard, the degenerative processes set in secondarily, and thus lead to further increases in the volume of the newly formed tissue by fatty degeneration, hyalin swelling, etc. The process begins in the vicinity of the media and is the first histologically demonstrable change in the diseased wall. As recently emphasized by Thoma, the combinations of the various degenerations are probably influenced by peculiarities in the general metabolism from even more diseases than those mentioned above. Faber, too, considers weakening of the intima the primary factor (see also Adami), while on the other hand Klotz considers intima hyperplasia from diverse causes (infections, toxins, increased blood pressure, etc.) the primary factor.

The author's conception of the pathogenesis of arteriosclerosis is as follows: if we start with the physiological thickening of the intima in the growing organism, we may view it, with Fuchs, as an expression of physiological adaptation (see remarks and lit. p. 98). The increasing quantity of blood requires that the wall be strengthened to maintain the necessary tension in the vascular tube. This strengthening is accomplished by thickening of the muscular media and by increase of elastic tissue in the intima; this latter tissue during years of use including increase of pressure, is able to develop to a certain maximum. If the possibility for further adjustment is exhausted, usually towards the end of the fourth decade, arteriosclerosis begins; the elasticity gradually diminishes from constant overstretching, particularly longitudinal tension; the addition of injuries such as infections and intoxications, make a substitute imperative and so the connective tissue is increased, especially in the intima, and this strengthens the wall by its high elastic resistance (Triepe). But such a compensation, although partly physiological, from age, is not permanent, and regressive changes such as fatty degeneration, calcification, hyalin degeneration, etc., are established in the thickened intima. Thus is developed arteriosclerosis in the narrower sense; later, the media is also involved. This idea applies, of coure, to arteries of the elastic type; in those of the muscular type, degeneration of the media and calcification predominate from the beginning, and there is no compensatory hyperplasia of the intima. There are, of course, exceptions to this rule.

### Special Etiological Requirements of Arteriosclerosis

The conditions vary under which arteriosclerosis develops, and probably not one, but many factors combine to injure the walls. Of greatest importance is perhaps, (*a*) *an abnormally increased functional demand.*

Others are:

(*b*) *Injury to the wall by infectious and toxic influences, nutritional and metabolic disturbances.*

(*c*) *Familial and hereditary predispositions.*

(*a*) The importance of increased demand is admitted by most observers (Thoma, Albrecht, Marchand, Jores, and others). Mechanical factors are also important; the excessive wear and tear of distension and high blood pressure are shown by the selection for changes of openings where friction is marked and pressure higher, or, as in sclerosis of the aorta, in front of stenosis of the isthmus, (p. 93), or, in the pulmonary artery with obstructions in the lesser circulation (lit. by Posselt, Hornowski), or in the splenic artery. It should be mentioned, however, that Thoma thinks not pressure increase, but slowing of the blood stream at the peripheral parts, is the active factor.

Arteriosclerosis is more frequent in muscular, hard working men than in women, and severe degrees are relatively rare in anemic phthisics. Cardiac hypertrophy may cause arteriosclerosis of the aorta and the pulmonalis. It is quite prevalent in those whose occupations entail heavy work, (sawyers, ship laborers, athletes, oarsmen); it is thought that the exceptional cardiac activity produces higher tension in the whole arterial system. Increased resistance in the overtaxed, tense muscles is also thought to increase arterial tension. Selective preference of arteriosclerosis for the coronary and splenic arteries is considered due to intermittent increase of tension, *i.e.*, resistance in the vessels, and the left coronary artery is more subject to this than the right, (Monckeberg). Abnormal fluctuations of vessel tonus from temperature differences, and even from purely nervous factors by way of vasomotor blood pressure increases seem to favor arteriosclerosis. Coffee and tea have been held responsible; hypertony itself with its consequences, is frequently considered the cause of arteriosclerotic thickening and narrowing of the renal arterioles, (contracted kidney,—see under kidneys).

Romberg, without more ado, calls arteriosclerosis, "a wearing out disease," supported, of course, by the increase of arteriosclerosis with increase in age. But age is only one factor; in purely senile conditions, the aorta is practically free of degenerative changes in the intima, but the wall, especially the intima, shows fibrous thickenings, dilatation and diminished elasticity, (Kani). But, on the other hand, according to Stumpf, even in earliest youth, physical forces are sufficient to cause minor circumscribed degenerative processes in certain parts of the aorta which may develop into arteriosclerosis. Arteriosclerosis in children (Simnitzky, Oppenheimer, and others) and in youth (see Monckeberg) surely cannot be considered a "wearing out disease," unless we assume that there is

absence of physiological thickening of the intima which permits normal blood pressure to act injuriously, or unless we suppose that increase of blood pressure is due to renal influences, or perhaps to high adrenalin content of the blood (Tornay, lit.); this would be premature "wearing out." Renal influences apply to many cases, including those of Stumpf. Finally, tissues can be injured by infections (see Klotz, experimental arteriosclerosis caused by functional overexertion, and compare to the contrary, Heusner, Schmiedl).

(*b*) Arteriosclerosis is also thought due to infectious diseases, such as typhoid fever, scarlet fever, measles, small pox, diphtheria, influenza, malaria (for doubts, see lit. by Arnsberger), gonorrhea, tuberculosis, etc., (lit. in appendix). The importance of infections has recently been reemphasized by Faber and Monckeberg. Experimental arteriosclerosis has been produced by injections of bacteria and bacterial toxins, (Gilbert and Lyon); Klotz was the first who used typhoid bacilli and streptococci in rabbits and obtained arteriosclerosis localized in the intima differing entirely from that induced by adrenalin (see below) and corresponding to the arteriosclerosis found in man by Jores. With diphtheria toxin, he obtained changes only in the media. Saltykow confirmed these results, (see Benda, Sumikawa). Apparently, therefore, bacterial toxins, and perhaps the bacteria themselves, are active causes of this condition, but the bacteria must necessarily be of low virulence, because virulent organisms cause verrucose arteritis (D'Antonia) or infiltrate the layers, especially the media, and produce necroses. Whether "aortite aigue," as it is called by the French (Hily, lit.), which sometimes causes sudden death, should be considered here, or whether it is only a first stage of common arteriosclerosis accompanied by organized thrombi (Marchand), is doubtful. Syphilitic arterial changes must be clearly and sharply differentiated from arteriosclerosis.

Although typical arteriosclerosis could not be obtained, nevertheless, severe necroses of the media were successfully produced in rabbits by the injection of adrenalin and other poisons; this encouraged further attempts to produce an alimentary arteriosclerosis in rabbits (by feeding them with liver), with somewhat similar results (Seersum, lit.). On the other hand, Anitschkow and Chalatow, Wacker and Hueck, and others (see ref. by B. Fischer) produced changes in rabbits similar to fatty degeneration of the intima in man, by feeding cholesterin supplemented by adrenalin, but Hueck himself is averse to applying these results to the pathogenesis of human arteriosclerosis. Furthermore, arteriosclerosis is frequent in metabolic disturbances such as gout, diabetes, adiposis, etc. As to intoxications, alcoholism is often held responsible (Bollinger), but its action is thought due to the effect of large amounts of fluid, (fluctuating blood

pressure, weakening of tissue). Direct effects on the intima have not been demonstrated. The author has seen confirmed alcoholics with normal, or, but slightly changed, arteries. According to Fahr, alcoholism favors arteriosclerosis via infection. On the other hand, it is frequent in lead poisoning, and many clinicians consider autointoxications, especially the intestinal variety, as factors (comp. Huchard); Faber shares this opinion. The excessive use of tobacco, especially of cigarettes, has been accused, (E. Hesse, Rehr, Beneke, Michels). Zebrowski and others claim to have produced aortic atheroma in this way in rabbits, but Schmiedl produced only necrosis of the media, (Beneke, Klotz). Obliterating endarteritis proves the influence of tobacco on the arteries, (see p. 120), but even in this condition, there is marked individual predisposition.

(*c*) According to the author's experience, arteriosclerosis may result from familial and hereditary factors producing tissues of subnormal nature (qualitative changes) or hypoplasias (quantitative changes). Hueck believes the hypoplasia, demonstrated in the cerebral vessels by Binswanger, who correlated it to juvenile arteriosclerosis, is due to deficient development of the muscular and elastic tissue, and too marked development of collagen. Hedinger thinks of nervous dispositions, tendency to disturbances of cholesterin metabolism, etc. (more lit. in appx.).

### Consequences of Arteriosclerosis

The arteries lose their elasticity, contractility, their firmness and resistance to tearing. The causes are the immobility of the hardened intima, the changes in the media, the destruction of elastic fibres and musculature with cicatricial substitution.

As a consequence, aneurysm (distension) of the arteries may result, especially of those not possessing firm beds, thus of the arch of the aorta. Small arteries (splenic, coronary, temporal arteries) become convoluted, dilated and lengthened. Arteries, early and uniformly calcified, may withstand distension. In comparison to the frequency of arteriosclerosis, aneurysm is rare.

Dilatation of the aorta and its branches produces a reversed action on the left ventricle which hypertrophies if the muscle is capable. Enlargement of the beginning of the aorta or involvement of its valves leads to relative or true insufficiency or true stenosis with their consequences, (dilatation and hypertrophy of the left ventricle).

The smaller arteries are often narrow or occluded, perhaps by thrombi (as in coronary sclerosis).

Other consequences are: (1) narrowing or occlusion of vessels, thus jeopardizing the nutrition of organs (encephalomacia) from (*a*) embolism from torn thrombi, debris or shreds from softened areas, (*b*) thrombosis,

known to have caused complete obliteration of the abdominal aorta (lit. by Schubart), (*c*) thickening of the intima. (*2*) Hardened or atheromatous, dilated and thinned vessels may rupture, especially when the media is destroyed (cerebral apoplexy). Sclerosis of the small and smallest renal arteries is exceedingly important in causing "true contracted kidney."

## Inflammations of Arteries

### Nonspecific Inflammations: (Productive, Purulent Arteritis)

**Productive Arteritis.**—Inflammations of arterial walls with proliferation and hyperplasia of connective and elastic tissues are frequent. According to the site of inflammation, we distinguish: endo-, meso-, or peri-arteritis. All layers are often involved (panarteritis) although possibly to different degrees.

(*a*) Productive endarteritis (eventually obliterating) is caused by proliferation of the cells of the intima resulting in thickening, narrowing, eccentric location of the lumen with final complete obstruction.

Microscopic study shows that the proliferation is essentially endothelial, especially of the fixed cells. Invasion of cells (leucocytes) from the outer layers of the vessel, *i.e.*, from the vasa vasorum, when present, is of little importance. When new vessels from the vasa vasorum or neighboring vessels invade the proliferating tissue of the intima, a veritable granulation is developed which may change into connective tissue. In the smallest arteries, obliteration from true intima proliferation occurs without the formation of new vessels.

Later on, a close network of elastic fibres develops in the thickened intima, partly by splitting away from the elastic membrane, partly by direct new formation, (Jores).

Productive endarteritis is quite frequent under many conditions, thus, in increased, decreased, or suspended intravascular pressure, such as the physiological occlusion of the umbilical vessels, especially the vein. This is better spoken of as physiological atrophy. According to Pfeifer, obliteration of the umbilical vein is caused chiefly by proliferation of the intima and new tissue growth within the lumen. As vascularization proceeds from the adventitia, the media atrophies and undergoes fibrous change. Thus the umbilical vein becomes a fibrous cord, but in some, a residual lumen is said to persist (Baumgarten). Again, according to Pfeifer, during closure of the artery, new elastic fibres in the media and the fibroplastic endarteritis form an elastic ring obstructing the lumen. According to Bucura, the lumen is closed by local contraction of the muscles, chiefly the longitudinal layer, (so-called cushion formation, see Bondi). (See p. 95, in reference to occlusion of Botalli's duct.)

Productive endarteritis is often a reactive-proliferative response to a stimulus from within, *i.e.*, hematogenous, *e.g.*, an embolus or toxin in the blood, or from without, *e.g.*, trauma, ligature, inflammation, etc. In other cases, as in the beginning of the aorta, ( productive endaortitis), it might be said to be engrafted or conducted by continuity from an endocarditis.

Endarteritis occurs in:

**Occlusion of Vessels after Trauma, Ligature or Suture.**—When an artery receives a small puncture wound, a spurious aneurysm is not produced (see p. 132), but the opening is closed by a thrombus of blood platelets, leucocytes and fibrin, protruding both within and without, (danger of embolism). The endothelium spreads over the margins, young

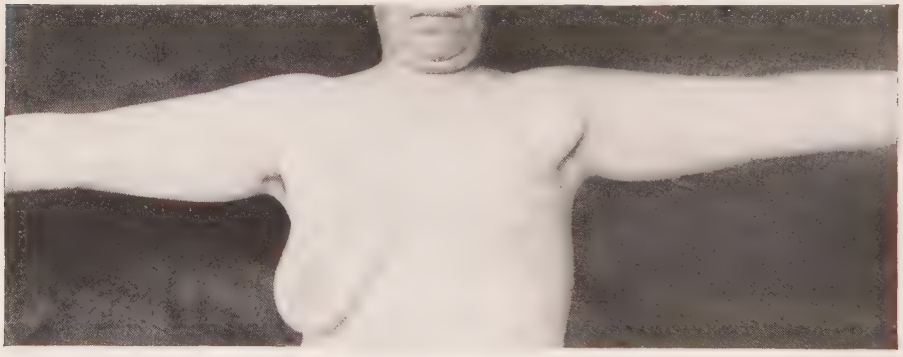


FIG. 57.—Approximately one inch of the brachial artery was resected in this case when an adherent mass of lymph nodes was removed from the axilla. Secondary carcinomatosis from a tumor in the breast. This illustration was taken 10 weeks after the operation. There was no swelling, discomfort, pain or other symptom referable to the arm. Ordinary suture material with no special care was taken in the resection of this artery. Sometimes thrombosis does not occur. L. H.

connective tissue proliferates from the various layers, but chiefly from the intima in close proximity to the endothelium, (Manz, Stich, and Foeppritz). Scar tissue is the end result; no new muscle cells appear in the media, nor can the elastic fibres, although new ones may be present, ever regain their original architecture as layers of elastic lamellae.

When an artery is crushed, torn, or even cut smoothly, as in amputations, the stump may retract so forcibly that the intima is folded and bleeding stops more or less completely.

Final occlusion is accomplished by productive endarteritis at the ligated end which is probably held shut by fibrin. In other, exceptional cases, a larger thrombus is deposited in the ligated stump, and if the vessel wall has been roughened by arteriosclerosis, organization of the thrombus occurs by productive endarteritis. The new vessels which appear have their origin in the vasa vasorum. Quite similar processes occur in veins.

In the aged, and in badly nourished individuals, proliferation of the intima and occlusion of the vessel is often very incomplete, (danger of secondary hemorrhage).

During the healing of an arterial suture, all three layers proliferate. The least active is the connective tissue of the media, while the intima shows abundant new growth of elastic fibres, (H. Jacobsthal).

Implanted sections of vessels heal without gaps, but the implantation is absorbed in time and replaced by the proliferating tissue of the recipient. (Lit. by Borst.)

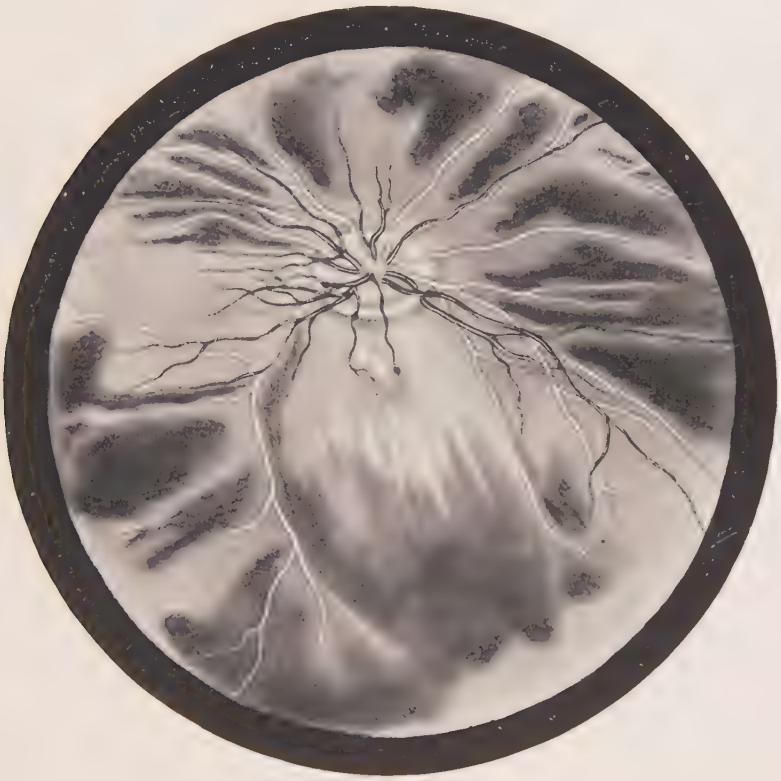


FIG. 58.—Hemorrhage in the right eye due to embolism of the retinal artery. This patient had puerperal sepsis and was admitted, having all symptoms of toxemia. She suddenly complained of extreme pain in the right eye and sudden blindness. Ophthalmoscopic examination revealed the arteries free of blood and hemorrhage present throughout the retina. Death two days later from sepsis. No change had taken place in the eye. L. H.

**Organization of Thrombi or Wedged Emboli.**— When thrombosis occurs in a vessel from ligation, external irritation, independent vascular disease, or slowing of the circulation, or when an embolus is firmly wedged in an arterial branch, the reactive productive endarteritis penetrates the thrombus or embolus and replaces it. Endothelial proliferation also occurs; according to Baumgarten it participates in the formation of con-

nective tissue, but this is disputed by Marchand, Muscatello, Merkel. There is an immigration of germinal cells from the innermost layers of the intima and finally, newly formed elastic fibres appear. (Jores.)

Partial occlusion from a thrombus attached only at one side of the vessel wall, or by an embolus which straddles a bifurcation without occluding the lumen initiates the same reactive processes in the underlying intima. The results are saddle, plate, net, or thread-shaped thickenings of the intima.

When obstruction by a thrombus or an embolus is complete, the end result may be complete cicatricial obstruction and contracting obliteration of the vessel, but sometimes, secondary new vessels lined with endothelium invade the occluding fibrous plug and render it patulous. Vessels penetrate the plug from the surrounding wall, but new capillaries enter from its free, endothelial covered ends. These vessels then enlarge and unite and the plug becomes patulous to the circulation. There may be channels within the thrombi which afterwards become widened and lined with endothelium. This process is called recanalization, or cavernous metamorphosis (Rindfleisch) of the thrombus or embolus, or sinus-like degeneration, because of its similarity of structure to the cavernous sinus of the dura, (Rokitansky). It is met in the aorta as well as in the smaller arteries, but is seen most beautifully in venous sinuses and large veins, (fig. 89). The lumen is filled with fibrous tissue showing old blood pigment, often perforated by gaping vessel spaces surrounded by a network of elastic fibres.

**Arteries embedded in inflamed tissue, as in the lungs,** testes, etc., are chronically involved by productive inflammation invading from without. All the layers undergo fibrous thickening (panarteritis), but the intima is most frequently, and most markedly changed, (productive endarteritis). Complete obliteration protects the vessels from rupture and hemorrhage. Good examples occur in old tuberculous cavities of the lung in which vessels passing through are the only remaining tissues. Acute purulent inflammations extending to arterial walls produce necrosis and quick rupture, or perhaps erosion aneurysms (p. 148).

4. Essential obliterating endarteritis as a cause of gangrene of the extremities is usually a sequel to thrombosis and organization (obliterating thromboarteritis), (see chapter "gangrene" under skin). It has been observed in pneumonia (Nielsen), in lues, etc. A non-leutic endarteritis obliterans was described by Winiwarter, and called "primary productive endarteritis" by Borchard; it is the cause of juvenile or so-called "presenile" gangrene of the extremities, sometimes symmetrical, and, as Erb states, causes intermittent limping with pain and weakness, (intermittent angiosclerotic dysbasia; lit. Bing, see also Idelsohn, Grube, Goldflam,

Oppenheim, Gerlach, and others). It occurs almost exclusively in men. Its etiology is obscure; abuse of tobacco, especially cigarettes (Schumann, lit.), diabetes, and hereditary predispositions, prediposition of the Semitic race, neuropathic diathesis, etc., have been mentioned. Sometimes its course is favorable, (see Oppenheim). The anatomical picture has been interpreted in various ways; lately, many assume that thrombus organization in arteries and veins is the essential cause. Buerger (productive thromboarteritis and phlebitis, or obliterative thromboangitis), points out that thromboangitis is frequently accompanied by a migrating thromboangitis of the peripheral veins, which is of diagnostic importance because of the peculiar skin nodules (former lit. by Thorel; comp. Blattner). For obliterative endarteritis with thrombus formation as the cause of gangrene of the extremities in malaria, see Almartine.

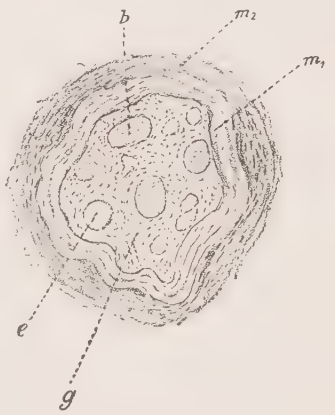



FIG. 59.—Recanalization of an embolus in a branch of the renal artery; g, organized embolus consisting of cellular connective tissue; within b, blood vessel with blood; e, empty blood vessel and other vascular holes; $m_1$, inner layers of muscularis with hyalin degeneration; $m_2$, outer layers of media blending with the adventitia (low power).

### Chronic Productive Mesarteritis

We discussed the mild degrees under (*a*). Secondary inflammatory disease of the media, chronic or acute, may accompany initial processes in the intima, (see under arteriosclerosis, and purulent arteritis, p. 122). Primary mesarteritis is very important in the infectious diseases, especially in syphilis with luetic aneurysms of the aorta (see p. 123 ff.), but it also appears in typhoid fever and is followed by thrombosis (Thayer), in puerperal infections with streptococci (McCrae), and in articular rheumatism (Klotz and comp. p. 63). We differentiate acute and chronic and productive mesarteritis; the latter leads to the formation of connective tissue in the wall.

Nodular periarteritis (Kissmaul and Maier) is the name given to a disease the nature of which is still under dispute. It is characterized by the formation of multiple, circumscribed, nodular, parietal thickenings in smaller and even microscopic arteries (of muscular type), in one, or many organ systems, (heart, mesentery, stomach, intestines, liver, kidney, extremities, etc.).

It is a destructive process finally involving every layer of the wall. Aneurysms and thrombi are common. The histogenesis is much debated. The picture varies according to its severity and duration. According to

Veszpremi and Janeso, granulation tissue grows from the adventitia into the other layers which have previously been infiltrated by fibrin and leucocytes. The vessel is therefore enlarged, and the destructive process soon extends to the intima. Others consider the intima the starting point, some, the media (Ferrari, Monckeberg). At any rate, there are necrosis and hemorrhage in the media, followed by leucocytic infiltration of all layers, especially the adventitia, (Benda). Gruber (lit.) who places the starting point at the border-line between media and adventitia, really adopts an opinion, not essentially different from the first. The disease may result in death by hemorrhage from ruptured aneurysms, or from peritonitis following localized necrosis of the kidneys and liver. But the process may be halted and healing take place by a fibroplastic inflammation replaced by scar tissue in the destroyed parietal areas; organization of thrombi, proliferation of intima and obliteration of the vessel occur simultaneously. Etiologically, an infectious or toxic origin is suspected. Verse (lit.) believes it is a special, rare form of syphilis of the vessels, but many others, such as Benda, Beitzke (lit.) Harbitz, Spiro (lit.), refuse to accept this view, (lit. in appx.).

As Frankel showed, the rose spots of typhoid fever display a peculiar disease of the finer (precapillary) arteries of the skin, which consists of hyalinization and necrosis of the innermost layers of the wall with proliferating processes chiefly involving the adventitia. It leads to the perivascular formation of circumscribed cellular nodules. These changes may be compared to the conditions in nodular periarteritis, but the typhoid nodules are specific, and permit in an excised rose spot a diagnosis which clinically is difficult. Similar foci appear in the brain, heart, all internal organs, and in the muscles. For this reason, Nicol speaks of a systemic disease of the small vessels (capillaries and precapillary arteries), but Ceelen and others found cell foci in the aorta as well, reminding them of the findings in syphilis, especially because they also followed the vasa vasorum in larger veins, (lit. by Eug. Fraenkel and Ceelen).

### Purulent and Gangrenous Arteritis

Pyogenic organisms invade the vessel wall (*a*) from the lumen, (*b*) from the neighborhood, or (*c*) by way of the vasa vasorum. The first may occur in any artery following metastatic attachments or embolic jamming of septic material originating in an endocarditis or in osteomyelitis, as in a case which the author observed in which there was severe arteritis with aneurysm formation in the pulmonary artery. It is more common, however, to see an infectious aortitis joining an ulcerative endocarditis,—progressing by continuity—or by contact with vegetations of the valves or detached particles, or from bacteria entering the coronaries and

reaching the wall of the first part of the aorta. Plaques, verrucose growths, ulcers, parietal abscesses and phlegmons of the wall are all possible. The changes in (*a*) progress like those in bacterial invasion of the cardiac valves. The organisms cause necrosis of tissue which becomes surrounded by a pyogenic area (ulcerative arteritis), on which thrombi are probably precipitated (arteritic thrombosis). The intima shows proliferating inflammation, resulting in obliteration of small vessels, or the arterial wall suppurates and becomes soft and friable. Rupture or aneurysmal dilatation is not uncommon, (acute infections, ruptured aneurysm). Schmaltz and Schmorl saw such infectious aortitis in diphtheria and angina; Vanzetti (lit.) saw several aneurysms of the thoracic aorta in pneumonia; (see also McCrae, Thayer, Stumpf, Rumrich, and lit. of infectious aneurysms, p. 148).

Arteries within suppurative or purulent surgical wounds soften and rupture, *e.g.*, the femoral, after an excision of an inguinal bubo; the left external carotid, following the application of a tampon of ferric chloride after extirpation of scrofulous nodes. Ulcerative foci which accompany scarlet fever, diphtheria, suppurative tonsillitis, not infrequently lead to fatal erosion of vessels, *e.g.*, the external carotid, and the lingual arteries.

Fatal erosion of vessels has occurred in a tracheotomy wound infected by diphtheria, or scarlet fever. The author made note of this in the inferior thyroid and in the external carotid arteries. Tumors also, after undergoing purulent change, may lead to the same result, (carcinoma of the tonsils or uterus).

### Specific Inflammations. Syphilis

Lues frequently injures arteries, the smaller (coronary, cerebral) as well as the largest (aorta). We may differentiate (*a*) changes occurring independently in the course of syphilis, and (*b*) those which appear within true syphilitic foci. In the latter, more frequent in smaller arteries, the vessel changes are often characterized by gummata which enter the wall from without, (comp. below). The most important changes, however, are in the aorta, occurring chiefly in the later stages and running a chronic course, as a rule. The picture is quite different from that of arteriosclerosis, and must be considered the result of severe focal disease in the vessel walls caused by the intensive action of the syphilitic virus, (Doehle, Heller, Puppe, the author, and others). It is a syphilitic productive mesarteritis which follows the vasa vasorum and causes focal destruction of the media with subsequent, more or less extensive, necrosis of the parts of the media between the actual foci of inflammation.

If the foci heal, they leave irregular, angular, fibrous scars in the media which may show macroscopic indentations in the intima, but frequently,

a secondary inflammatory-regenerative, purely fibrous, cicatricial thickening of the intima is added to this change in the media, and this often dominates the whole aspect macroscopically, and covers the destruction of the media. It persists for some time as a bluish white, scarred thickening, but is prone to undergo further degenerative changes especially atheroma, thus wiping out, more or less, the characteristic macroscopic picture, (combination of mesarteritis with arteriosclerosis 112).

In typical cases, the change presents pitted, radiating depressions with thinning of the wall, and coarser, angular, sunken areas as though hammered out. Some parts are tendon-like, finely wrinkled, with flat surfaces, or with plateaus of cicatricial, bluish white plates. At other places, there are diffuse, cicatricial, uneven scars of pale gray, or bluish white tint in contradistinction to the normal yellow aortic inner surface.

FIG. 60.—Syphilitic aortitis (mesaortitis); pitted angular depressions (punched out) in the ascending aorta of a young syphilitic woman; valves intact; aorta otherwise unchanged; about $\frac{3}{4}$ nat. size.

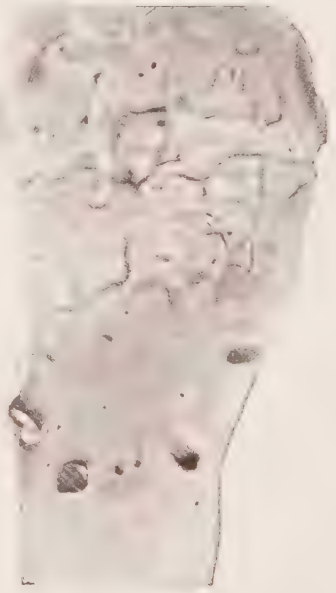


FIG. 61.—Syphilitic mesaortitis; sudden transition of the severely changed thoracic into the intact abdominal aorta; 38 year old man (from the same; aneurysm in ascending aorta, fig. 81); $\frac{2}{3}$ normal size.

Frequently the change is confined to only one area, or to a few places, in which cases the first part of the aorta is preferred; the valves may be normal, or markedly changed. When changed, there may be insufficiency because of extension of the aortic disease to the valve attachments, and the sinus of Valsalva, or to the margins (marginal thickening, Lupu). But the valves as a whole are often thickened, stiffened, shortened or even adherent by their margins, or are flat with the pockets obliterated to the wall of the aorta, (see also Fabris, Bozzolo, Engel). Even though unchanged themselves, they may become too short for the dilated aorta, (relative insufficiency).

The coronary arteries are sometimes narrowed, and one may eventually be occluded. Sometimes the foci form a belt in the beginning of the aorta, but they may reach as far as the thoracic aorta, and to the diaphragm, *i.e.*, the beginning of the abdominal aorta, and then stop quite suddenly. This border is rarely crossed in continuity, even if isolated areas are seen in the abdominal aorta. The diseased part as a whole is thick-walled, inelastic, usually dilated and lengthened; more rarely, it is somewhat smaller than normal.

The openings of large branches from the arch are occasionally narrowed or blocked by scars in the intima so that the radial and carotid pulses are absent, (comp. Fahr, Toppich). The branches themselves, as a rule, remain completely free of disease, (see Beneke).

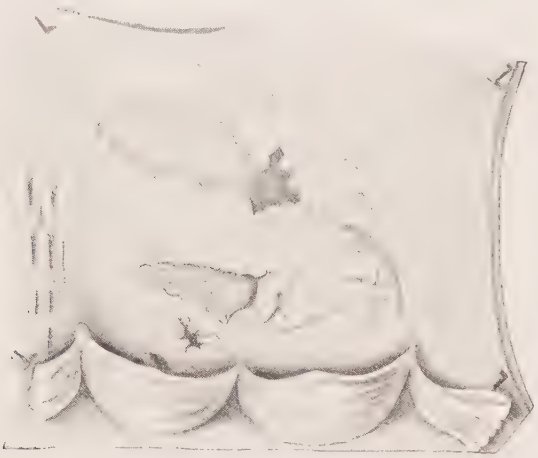


FIG. 62.—Syphilitic aortitis (mesaortitis); pitted contractions and depressions (punched out) of the aorta of a syphilitic man 53 years old, with fibrous orchitis; valves intact; the aorta otherwise free from changes; ¾ nat. size.

Especially characteristic are those cases in which an exceedingly severe change is sharply confined to a relatively small area; this can never be mistaken for common arteriosclerosis, especially if the individual is young (20 to 30 years old), although it has been seen in individuals of seventy.

In the latter cases, but sometimes earlier also, as the author saw in a paralytic 52 years old, the picture is complicated by severe atheroma, (p. 124).

Syphilis of the aorta is quite frequent. Stadler (lit.) found it in Leipzig, in 82% of over 200 cases of lues; Chiari in his material found it in 59%, Oberndorfer in Munich, in about 7% of all cadavers. According to Romberg, it is a later visceral luetic involvement, but exceptionally, may appear in the first two years, as in Liek's case, in a student 26 years old, occurring 7 months after infection, (see also Saathoff). Congenital lues

(p. 131) is also supposed to cause early mesaortitis (see Lippmann, 17 year old youth).

Occasionally, other luetic changes are found at autopsy, especially gummata in the heart, testes, brain, liver, etc. But it is important to remember that they may be absent; indeed, this is more frequently the case, (see Beck, Bauler, material at Basle).

In progressive paralysis, aortic lues is said to be relatively frequent. Straub found 69 in 85 cases of paralysis; this percentage is probably high, and generally, aortitis in paralysis is probably no more frequent than in lues as a whole, (Chiari, Lenz; see also Ginsburg).

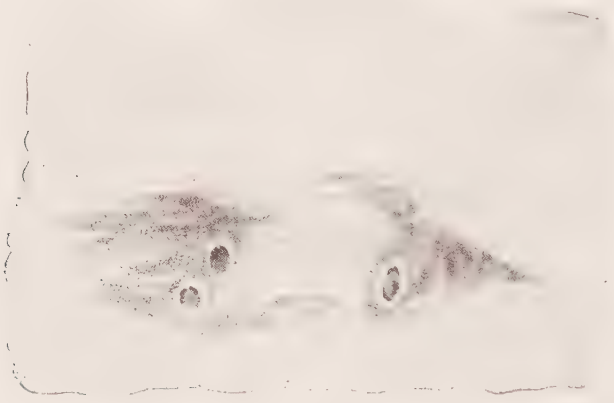


FIG. 63.—Gummatous aortitis (mesaortitis); intima thickened, sclerotic, finely wrinkled (low power); (see Paul Beck, Gummatous Aortitis, I. Diss. Basle, 1903).

In tabes, statements vary between 9% (Nordmann) and 58% (Arrulani, see also v. Strumpell); Hubert found 54 tabetics (25%), among 220 cases of aortic lues.

The most important clinical symptoms in lues of the aorta, appearing in about one-half of the cases and almost always ending fatally are (*a*) angina pectoris (see Gruber), due especially to involvement of the openings of the coronaries (see Curschmann); (*b*) aortic insufficiency, and (*c*) aneurysm. Men are more subject than women; thus in Beneke's series there were but 24 women to 148 men. It must be remembered that greater functional demands are asked of men and this plays a role in addition to the infection, (Romberg). To explain the preference of the thoracic aorta over the pelvic part, we must remember the more extensive physical lesions there. The time between infection and subjective symptoms varied in Beneke's patients between 5 and 44 years. The average was 20 years, and the average age of the patients, 43 to 45 years. For more numerical data, see Benary, Citron, Hubert. See Schottmuller, Baetgo, Hubert as to the beneficial influence of antiluetic treatment.

Syphilitic mesaortitis may take the form of gummata—gummatous mesaortitis—while in other cases, the small cell infiltration and the productive inflammation tending to connective tissue formation show no specific signs, although etiologically they are related to lues. Indeed, in the same case, may be found the round cell infiltration and simple and gummatous granulations. The inflammation has a tendency to cicatricial change, and the gummatous foci also show a tendency to scar formation.

If a marked secondary fibrosis of the intima is added, it can properly be called fibrous—or cicatricial, syphilitic aortitis.

The gummata consists of round cells, epitheloid and spindle cells and, frequently, numerous giant cells, while they may show necrosis in the centre (caseation). They are in the media, and sometimes also in the adventitia. They are found but seldom in typical arrangement and were already mentioned by Doehle, Heller and others, but described in detail by Heine (Benda), Fabris and the author, (med. ges. Basel March 1903, diss. Beck). The specificity of the change was thus demonstrated histologically, (comp. Fahr and Widemann, Nauwerck, Steinmeier). Usually we find but simple cell infiltrations, often perivascular, consisting of lymphocytes and plasma cells in varying proportion (Fukushi), or vascular granulation tissue foci with variable cell abundance, and jagged, map-like cicatrices especially in the media. Corresponding to these foci, the lamellae of elastic fibres of the media are interrupted and destroyed. Between the foci are islands of necrotic media with, here and there, foreign body giant cells lying in close contact with the necrosis. The adventitia is infiltrated, focally or diffusely, with round cells; later it is thickened by connective tissue proliferation. The vasa vasorum have a tendency to occlusion from proliferation of the intima, plus small cell infiltration in their adventitiae. Demonstration of spirochetae is not promising; isolated findings were first reported by Reuter, Schmorl, Benda; but Wright and Richardson succeeded in showing them in half of the cases, in two of which the infection was 16 years old. Many experienced research men have failed completely. Only very young foci promise a chance, (lit. by Fukushi). The change may, in all probability, be interpreted as luetic in most cases, even though neither spirochetae nor typical gummas can be demonstrated in the media; the whole case must be taken into consideration and other luetic signs searched for, otherwise it might be confused with aortitis of other infectious origin, (see p. 115). Usually, tuberculosis is easily excluded. Circumscribed foci of fibrous type caused by trauma would probably not, according to Feich's opinion, lead to mistakes. The macroscopic diagnosis may be made difficult by: (*a*) a combination with true arteriosclerosis and atheroma, not only in advanced age, but, as the

author saw, even in the fourth decade, which is, however, exceptional. In such cases the abdominal aorta, as well as the larger branches, are free of luetic changes, but are arteriosclerotic. Difficulty of diagnosis may be also encountered, (*b*) when secondary thickening of the intima is established over the areas changed by mesarteritis, provided that, as in the most pronounced degrees of the inflammatory degenerative media changes, atrophy of the intima and aneurysmal bulging have not previously occurred. We must differentiate this regenerative process which is mainly fibrous, from the purely hyperplastic thickening of the intima in arteriosclerosis, in

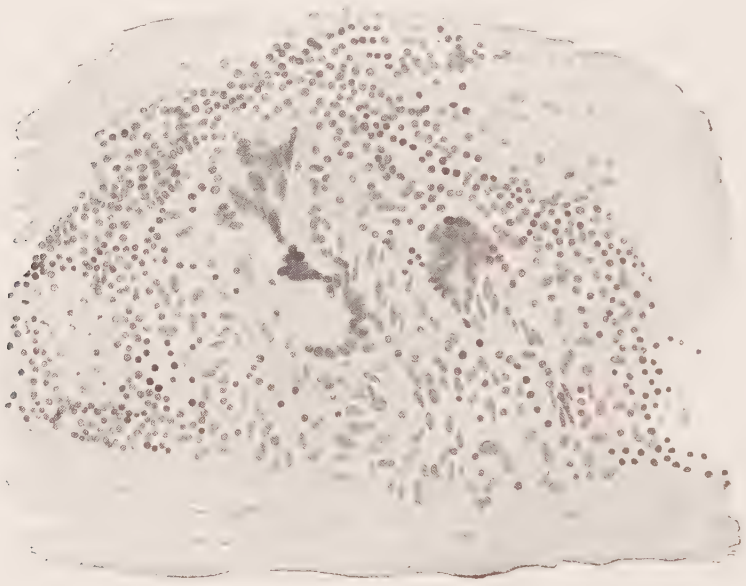


FIG. 64.—Gummatous area in the media in gummatous aortitis; giant cells, epithelioid cells' round cells, necrosis (high power). (Paul Beck, I. Diss., Basle, 1903.)

which there is an abundance of elastic fibres. Others, (see Adami), consider it compensatory, and thus similar to the latter process. It usually is a cellular, stormy, irregular, inflammatory proliferation, (see D. Antona, Eug. Fraenkel). The intima thickening: (1) shows tendency neither to calcification nor atheroma, but is tendinous, bluish white, stiff, scar-like or wrinkled in fine folds, or is grayish white, smooth, cartilaginous, nodular, with plateaus often several millimeters high, such as are scarcely ever seen in arteriosclerosis; or (2) regressive changes take place (atheroma, calcification) in which the intima is but slightly thickened. Multiple thrombi are rare (Moriani).

Eug. Fraenkel and Much, Nauwerck a. Weichert, Pick, Fich, Guladse, Gruber and others, advise the Wassermann reaction on the cadaver in

doubtful cases. If everything else points to the luetic nature of an aortitis, the Wassermann test is valuable as a means of confirming the diagnosis, (experiments by Vanzetti).

According to the conception of the author as to the relation of the changes in syphilis, the nomenclature varies. While Heller and the author speak of syphilitic mesaortitis, others, at the time this affection was considered parasyphilitic, spoke of productive mesaortitis (Chiari), or cicatricial sclerosis of the aorta (Moenckeberg and others). This latter appellation is, however, misleading, since we have a certain conception in view in arteriosclerosis, *i.e.*, degeneration of the intima. But a scar is usually the consequence of a productive inflammation. If an indifferent name is selected for cases in which specific syphilitic products are no longer present, then it would be better to speak of fibrous, cicatricial or productive aortitis.

We can only agree with Kulbs, when he desires that anatomists pay a little more attention to other parts of the vascular system besides the aorta, in cases of syphilis, (comp. under gangrene of extremities, p. 120).

When typical cases of luetic aortitis are examined, it becomes apparent that only a small step separates them from circumscribed aneurysms.

In the earlier stages it is quite common to see beginning bulgings, but, on the other hand, the author saw cicatricial syphilitic aortitis in 60 and 70 year old individuals in whom no such aneurysm formation was present; in fact, this latter circumstance is far more frequent.

Larger aneurysms with extensive gummatous caseation of the wall, are quite rare, (see case, Risel).

In the smaller arteries, and this is especially applicable to the basal arteries of the brain, there may be differentiated two main types which can be briefly designated as: syphilitic arteritis, and gummatous arteritis. There are transitions between them, and both begin in the outermost layers.

The cerebral arteries are often affected in the very early stages of lues, usually simultaneous with the meninges.

(*a*) In gummatous arteritis (Baumgarten), nodules with caseous centres, a fibrocellular periphery, and giant cells appear in the adventitia and perivascular lymph sheaths. The gummatous granulations invade the adventitia and media, and the intima often proliferates so markedly that occlusion occurs, (luetic obliterating endarteritis, Heubner). But this proliferation may prevent the formation of aneurysms, which occasionally begins at once. Sometimes the change is found independently, especially when vessels pass through gummatous foci, although it is rare and best seen in the basal cerebral arteries, especially in gummatous meningitis. In most cases, however, the vessels passing through syphilitic foci show only

a common periarteritis and endarteritis, (see fig. 65 and comp. the picture of gumma of muscle under muscles).

(*b*) Syphilitic arteritis is not uniform, and not definitely characterized. There are probably always changes, *i.e.*, infiltrations and finally granulomatous nodules, in the adventitia and perivascular lymph sheaths of the cerebral arteries, and usually there are syphilitic changes of the meninges. In some of the cases we see at once a luetic obliterating endarteritis, *i.e.*, cellular proliferation of the intima finally leading to obliteration (Heubner), while the media is almost unchanged, (see also Schroeder). In other cases, the vessel wall and its lymph sheath are diffusely infiltrated, (panarteritis), leading acutely, to dense cellular infiltration combined with necrosis of the media. This may be accompanied by fibrous exudation

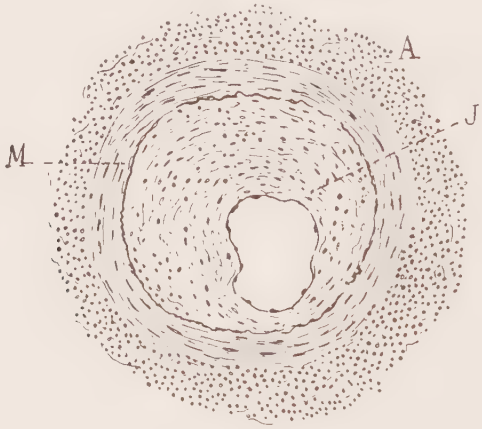



FIG. 65.—So-called endarteritis obliterans of a basal cerebral artery in gummatous meningitis; A, adventitia, cellular infiltration; M, muscularis free; J, thickened intima of cellular fibrous character; lumen eccentric (low power).

progressing as far as the intima and ending with scars in the media, and endarteritis with its tendency to obliteration; or, a chronic granulation tissue growth gradually causes more or less fibrous change in the vessel walls, (fibrous panarteritis), which also eventually leads to total obliteration, or thrombosis, or the formation of aneurysms. Chiari could demonstrate luetic endarteritis in a congenital syphilitic female child, 15 months old, (Heubner).

To differentiate between syphilitic arteritis, especially that mentioned under (*b*) and arteriosclerotic changes, the following may serve:

In lues, (1) the individual is frequently young and shows other signs of syphilis. (2) Only a short section of the vessel is affected, possibly with an otherwise, quite intact, vascular system. (3) There is a tendency to obliteration and fibrous metamorphosis, but no inclination to atheroma and calcification. The diseased part of the vessel, *e.g.*, a section of the basilar

artery, may be hard and white and changed into a solid cord, or may contain an eccentrically placed lumen. (4) The actual participation of the adventitia in syphilis is of histological importance, (lit. by Verse).

Purely histological investigation of other forms of obliterating endarteritis may give rise to difficulties, as in parasitism, (see there), tuberculosis of the soft meninges, (see Durck, with discussion), and nodular periarteritis, (see p. 121).

*Aortitis in Congenital Syphilitic Children.*—According to v. Wiesner, Bruhns, v. Wiesner and Rach, who, however, rarely found spirochetae in syphilitic fetuses or in children who died during birth or shortly afterwards, among other things, are inconstant small cell infiltrations in the aorta with connective tissue proliferation especially at the border of media and intima. Wiesner believes strongly in the specificity of these findings against all the objections of Scharpff, and the former is verified by Klotz and by Rebaudi (lit.) who found spirochetae in 5 cases out of 13. See Neugebauer, as to changes of the aorta in congenital syphilis. (Lit. in ref. to syphilis of arteries, especially of the aorta in appx.)

## Tuberculosis

Tubercles in the intima caused by invasion from the blood, are rather rare in the large arteries, and probably best seen in the pulmonary artery or aorta. They may become the starting point of general miliary tuberculosis.

It has been said that atheroma makes the aorta vulnerable to infection, but the author saw tubercles in smooth aortas, even of children.

Tubercles are frequent in the intima of the renal arteries and are followed by anemic infarction or by disseminated nodules. The endothelium proliferates actively; nodules contain giant cells and tubercle bacilli; caseation and disintegration occur.

If an artery passes through a tuberculous area, it may be invaded from without, either in discrete nodules or diffusely, and later caseation causes hemorrhage.

This is often a symptom of beginning pulmonary tuberculosis; in later stages, the hemorrhages come mostly from ruptured aneurysms in the cavities, (see under lung). Even in the aorta, perforation or aneurysm formation has occurred from tuberculous proliferation near the vessel and invasion of the wall from a neighboring lymph node, (Bauer, rupture; Girardet, perforation into aorta and trachea); or, as in a case of spurious aneurysm of Vanzetti, from vertebral caries. In all such cases, the aneurysms are spurious. In tuberculous meningitis, an elongated rounded swelling of the vessels from tubercles which come from the sheath of the

adventitia is especially typical. The intima may be thickly infiltrated by round cells.

See Vanzetti (lit.) on the histology of blood vessel changes in experimental tuberculous foci and the formation of aneurysms.

3. Arterial actinomycosis is very rare. It has been complicated by aneurysm of the pulmonary artery, (see Reiche).

## Aneurysms

(LIT. IN APPENDIX)

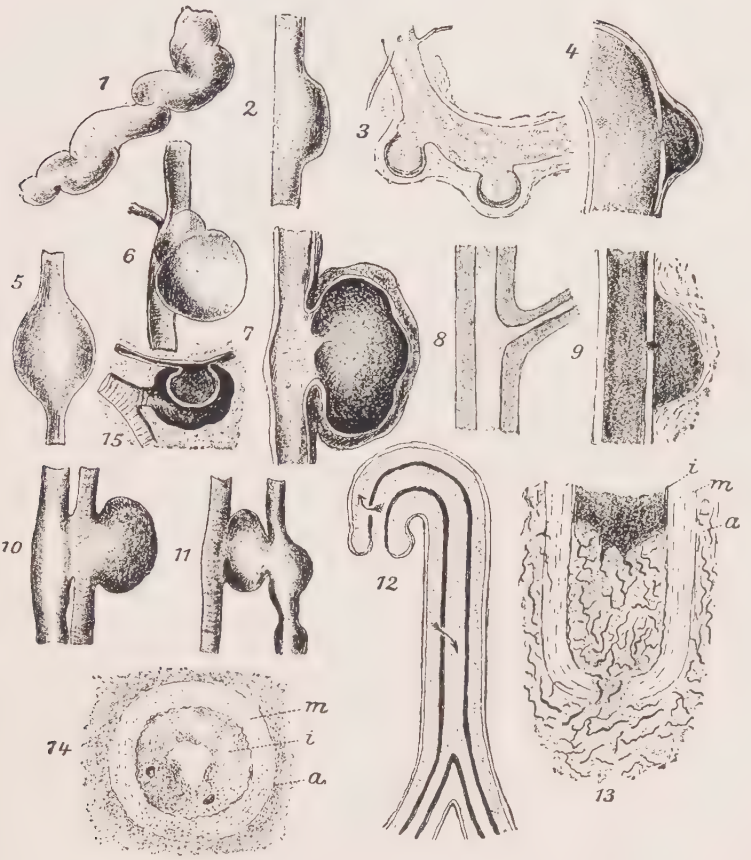
An aneurysm is a dilatation of an artery due to changes in its walls. It may be diffuse (arteriectasis), or circumscribed, or transitional between these two.

According to Pommer, there is a fundamental difference between arteriectasis and aneurysm, although they may accompany each other, and aneurysm may develop from arteriectasis. Aneurysm is characterized by solution of continuity of the elastic tissue of the media, (p. 137); arteriectasis is caused by thinning of the media.

Aneurysms may be divided into the true and false. In the true type, the diseased vessel wall, or the wall of the aneurysmal sac, can still be recognized as parts of a vessel. In pseudo-aneurysm, blood leaves the artery after traumatism or disease, and burrows a channel through periarterial tissue, so that the resulting hematoma, at first diffuse, is later confined by surrounding cellular tissue and becomes encapsulated, as it were, in a sac which communicates with the artery, but in its essential structure, is no part of the vessel, (fig. 9, p. 133).

Traumatic pseudo-aneurysms are caused by stab wounds, squeezing, bullets, etc. If the opening is in but one side of the vessel a space is formed surrounded by proliferating adjacent connective tissue and appearing like a huge bag at some circumscribed part of the vessel—circumscribed pseudo-aneurysm, encapsulated hematoma. The tear may be closed later by a thrombus, and be filled via a productive arteritis, but it frequently persists as an opening, permitting communication between the sac and the vessel. If the blood distends the cystic sac more and more (sometimes enormously so), it may prevent definite encapsulation and histological "ripening" for many months, (see Justi). According to Bier, the author's personal observation, etc., the picture presented in the early stage is as follows: the blood in varying amounts coagulates and diffuses into the adjacent tissue. If the dark clotted masses are removed, there is found in close proximity to the opening in the vessel, a relatively small globular or cup-like cavity, communicating with the vessel lumen and filled with fluid blood (coagulated in the cadaver). The cavity is a mold

of the clot of the hematoma and usually presents a somewhat lighter, delicate, and frequently laminated, membrane-like lining which is con-




FIGS. 66–80.—1, Cirsoid aneurysm; 2, boat-shaped aneurysm; 3, miliary aneurysms of a cerebral artery (microsc.); 4, sacculated dissecting aneurysm, intima torn; 5, spindle-shaped aneurysm; 6, sacculated aneurysm of the basilar art., nat. size; 7, sacculated aneurysm of the aorta, cross section; 8, brain capillary with blood in the surrounding lymph sheath (microsc.); 9, pseudo-aneurysm, due to puncture of the vessel wall; 10 and 11, two forms of arterio-venous aneurysms caused by common injury to artery and vein, in the first: vein communicates with artery, arterial blood bulges the vein; the artery with twice punctured wall, shows an aneurysm; in the second: an aneurysmal sac, between artery and vein, empties into the vein, saccular dilatation of the latter is superimposed which led to the diffuse phlebectasia (according to O. Weber); 12, diffuse dissecting aneurysm in the aorta to within the iliacs. The upper arrow leads through the tear in the intima into the pseudo-channel the lower arrow from there back into the inner lumen (diagramatic); 13, ligated artery, organic closure after organization of the thrombus by vascular connective tissue; lumen of artery and vicinity of stump surrounded by vascular connective tissue; i, intima; m, media; a, adventitia; 14, tuberculous arteritis; a, infiltrated adventitia; m, media, partly hyalinized, partly infiltrated; i, intima with tuberculous proliferation, partly caseated; 2 giant cells within; 15, aneurysm of the pulmonary artery projecting into a small cavity, communicating with a bronchus (diagramatic).

sidered by some as a product of the distension, *i.e.*, a quickly formed thrombus at the tearing place composed of platelets and fibrin, (among

others, see Kallenberger; lit., Hedinger). According to Bier, however, it arises from the hematoma itself by pressure of the blood circulating in the cavity. The author thinks the latter conception is more probable, with the modification, that the fibrin membranes showing platelet scaffolding, and inflammatory complications, including abundant leucocytes are partly secondary deposits from the blood stream and therefore, of thrombotic nature. Later, when the coagula in the hematoma have been partly absorbed and partly organized by granulation tissue, the lining membrane of the sac also becomes organized and blends with its surroundings, thus forming a firm connective tissue mass. It then becomes like a true aneurysm, in that the blood circulates through it. Bruits may also develop. Thrombi, laminated like onions, (mostly fibrin), may eventually line the sac and even fill it. If the orifice closes, the cystic sac may be isolated from its surroundings, and its true nature is difficult to determine, especially when, in the course of time, its contents become altered, and are not bloody, but serous. The smooth inner surface may contain brown pigment for long periods. (War aneurysms, see Justi, M. B. Schmidt, and exhaustive literature up to 1919, by Stich and Fromme.)

The following is an accepted classification of true aneurysms.

1. True spontaneous aneurysms.
2. True traumatic aneurysms.
3. Dissecting aneurysms (between true and pseudo-aneurysms).
4. Embolic aneurysms (*a*) simple, (*b*) infectious or mycotic.
5. Erosion (ulceration) aneurysms.

We must also discuss arteriovenous and congenital aneurysms.

### True Spontaneous Aneurysms

They assume various shapes, and accordingly, we differentiate the diffuse, cylindrical and circumscribed types. In individual cases we speak of saccular (p. 133, figs. 4, 6, 7, 10), boat-shaped (fig. 2), or spindle-shaped (fig. 5) aneurysms. If several spindle-shaped aneurysms lie close together in a vessel, a complex fusiform mass is produced. In circoid aneurysms (vine-like) the artery is distended and lengthened, consequently convoluted; this form is most frequent in the splenic artery, (fig. 1, p. 133). The circumscribed saccular variety is the most important form of spontaneous aneurysm, (p. 133, figs. 3, 6, 7). The sac is rounded or elongated, and often possesses secondary and tertiary bosses. They vary much in size, and, according to Eppinger, may be as large as a pail, but are usually no larger than a fist.

Diffuse aneurysms are also called dilatation aneurysms, *i.e.*, the vessel wall, *e.g.*, the arch of the aorta, in consequence of parietal changes (arteriosclerosis, cicatricial aortitis, etc.) is too weak to resist the blood pressure

and distends two fold or more. The circumscribed saccular aneurysm is either a dilatation aneurysm with a wide opening with no constriction, the sac is not much wider, no thrombi, or a rupture aneurysm, *i.e.*, the media ruptures at some circumscribed area destroyed, *e.g.*, by syphilis. In dilatation aneurysms, the wall first consists of all three layers, but their structure becomes more and more indistinct as the media undergoes changes, especially the tunica elastica, (Eppinger). On the basis of 24 cases, the author found that in arteriosclerotic aneurysm (*a*) the degeneration of the media which leads to fibrous hyalin changes always progresses in a flat tape-like manner from the inner layers outward, while (*b*) in syphilitic aneurysm, scattered mesarteritic foci and scars are predominant. In (*a*) the adventitia is infiltrated and the intima is always thickened and finally atheromatous; in (*b*) it is occasionally thickened secondarily, (for more details see Amenomiya). As the sac enlarges, the media, of approximately its former thickness, shows increasing fragmentation and thinning, until it is completely replaced by connective tissue derived in part from the sclerotic, dense, thickened adventitia. Then the normal parietal structures are recognized with great difficulty. Finally, the thickened adventitia is the only structure offering resistance to the increasing distension, assisted to but slight extent by an augmented thickening of the intima and by the fibrosed media. Frequent calcification of parts of the wall also contributes to strength, especially in the arteriosclerotic variety, but the increase in size of these fibrous sacs proves that the connective tissue is unequal to the task. Bone formation within the wall is rare.

If the wall is unable to compete with the increasing dilatation, the aneurysm ruptures, unless adjacent parts remedy the defect, or a new sac is formed by the reactive connective tissue proliferation of soft tissue in the vicinity, (spurious aneurysm).

### FORMATION OF SPONTANEOUS TRUE ANEURYSMS

The beginning of an aneurysm usually corresponds with the time of beginning arteriosclerosis, *i.e.*, during the fourth decade, but it may occur sooner or later.

In the majority of spontaneous true aneurysms, arterio-sclerosis and atheromatosis or arteritis are responsible; syphilitic mesarteritis is probably the most important and commonest etiological factor in the sacculated, and the multiple aneurysms of the aorta as well as in those of its larger branches, especially the innominate artery.

While the responsibility of syphilis in causing aneurysms of the larger vessels was formerly denied, (Schrotter, as late as 1899), today it is so well accepted, especially since the recognition of syphilitic aortitis (see Heller,

Malmsten, Benda, Bauler, lit. Bozollo, Allan, and many more), that some practically deny that arteriosclerosis and other factors ever play a part, (see Hofrichter). Still others estimate that syphilis has a share in 80% of the aneurysms in the thoracic part of the aorta, (Malmsten; 82% Hampeln; 92% Rasch). The author's investigation of 24 aneurysms of the aorta in Basle (I Diss. Bauler) yielded the information that an equal number were due to arteriosclerosis, but since the subjects were all quite

FIG. 81.—Syphilitic aortitis with saccular aneurysm, size of a chestnut extending into the posterior sinus of Valsalva; thrombi within; valves intact (a second aneurysm in the descending aorta, size of a cherry, had perforated the left bronchus); death from hemorrhage and asphyxia. Same case as fig. 61, 38 year old brakeman; ⅔ nat. size.

elderly, the share accredited to arteriosclerosis was probably somewhat too large. If, as was formerly assumed, arteriosclerosis is the chief factor, aneurysms of the aorta should be far more frequent, considering the prevalence of arteriosclerosis. Arteriosclerosis, however, is of great importance in the diffuse aneurysms of the abdominal aorta, the spindle-shaped aneurysms of the iliacs, and the circoid aneurysms of the splenic artery.

Finally, the syphilitic etiology is less important in the aneurysms of small and smallest arteries which, according to Klotz, are found as miliary swellings of the peripheral vessels in approximately one third of all people over 50 years of age. This also holds true for aneurysms of the basal arteries (see Kerppola), most frequently in the anterior communicating branch, (Busse; see also Benda).

All spontaneous true aneurysms, in the final analysis, may be traced back partly to inflammatory-productive and partly to degenerative changes in the media, which offers the chief resistance to the blood pressure. The changes, principally in the elastic fibres, were pointed out quite early by Koster, and his pupil, Kraft. They described mesarteritic foci which broke the continuity of the elastic fibres and which led to the formation of fibrous foci. V. Recklinghausen and Helmstadter also describe the tearing of elastic fibres, and Manchot saw connective tissue production at these places. Comment may be made on the frequency, even in young individuals, of convoluted temporal arteries, which, according to M. B. Schmidt, is due to rupture of the internal elastica and the adjacent muscularis from "constitutional inferiority" of this layer. These foci in the media become pliable and thus favor dilatation which increases the pulling and rupture of fibres until the intima is also involved. Kerppola, while investigating aneurysms of the basal arteries, found splintering and granular decomposition of elastic fibres and fat infiltration and necrosis of the muscle elements.

Since, in lues, the aorta especially, exhibits such frequent mesarteritic processes and their calloused residues, the frequency of aneurysms of this vessel is easily understood, although of these forms of aortitis only a fraction is followed by aneurysms, (comp. Baer). Indeed, reports have been appearing for some time in reference to cured (?) aneurysms in younger luetics by antiluetic medication, (St. Etienne, Muhlhaus; comp. p. 126). It must not be forgotten that other infectious processes which cause arteritis may also cause aneurysms, although doubtless quite infrequently. Those named under arteritis (see p. 115 etc., also p. 122), and articular rheumatism (Renon, Weil and Menard) may be mentioned. Even tuberculosis has been held responsible, (Heller). According to Thoma, in arteriosclerotic aneurysms, the primary change is a non-inflammatory alteration of the media consisting of diminished elasticity and rupture of the elastic fibres. Subsequent to this weakening, the media and then the vessel wall as a whole, have a tendency to stretch. A compensatory endarteritis attempts to keep the lumen at its original caliber and to strengthen the wall by thickening the intima, with arteriosclerosis as the result. If this does not succeed, *i.e.*, if the changes in the media proceed too rapidly, the compensatory hypertrophy of the intima cannot keep pace, and a

dilatation, or a rupture aneurysm develops. In the latter, the intima tears over the pliable media, from excessive tension even if thickened, because it is then too unyielding to follow, elastically, the tendency of the media to dilatation. Rupture produces the so-called dissecting aneurysm. Injections of adrenalin (0.1 to 0.3 mg. of the commercial 1–1000 solution) into rabbits, continued for some time, frequently cause necrotic foci in the media of the aorta and larger vessels which eventually calcify, (lit. in appx.). The thinned wall bulges through these parchment-like, white foci forming saccular as well as dissecting aneurysms. The beginning change is degeneration of the muscle fibres, the nuclei of which disappear; later, the elastic fibres of the media also disintegrate. Connective tissue proliferation may then occur in the vicinity of the foci and also in the intima. Necrosis of the media with calcification naturally is not a mesarteritis, as some say incorrectly, and for this reason there is no analogy with luetic arteritis, nor with arteriosclerosis. But these experiments do permit the deduction that toxic substances may severely injure the vessel wall, and this knowledge can be applied with due caution to human pathology, especially to calcification of the media. The same experimental results have been obtained with many other substances, (lit. by Benecke, Saltykow, Fleisher, Meyer, Otto).

### THE SITE OF TRUE SPONTANEOUS ANEURYSMS

True spontaneous aneurysms are found most frequently in the aorta, (arch and thoracic), including the largest which ever occur. Next in frequency are the popliteal, femoral, carotid, subclavian, innominate arteries (lit. Hofrichter).

Aneurysms, especially of the aorta, occur much more frequently in men than in women; 108 men to 75 women (F. Muller). Among 58 cases in the pathological institute in Basle, (9570 autopsies, see I. Diss. Bauler), the author found 37 males and 21 females, but the cases in young individuals were equally divided between the sexes; the same holds true of the very rare aneurysms of the pulmonary artery, with the exception of cases of pulmonary phthisis, (lit. Henschen, Posselt, Ploeger). In a 79 year old woman, the author saw a rosary-like, diffuse, aneurysmal dilatation of all branches to the pleura; the vessel was partly filled by thrombi and the large branches were as thick as thumbs (comp. Pick's case). As to the rare aneurysms of the sinus of Valsalva, see lit. by Sommer, etc., p. 148. Aneurysms are said to be more frequent in certain countries (England, America); in others (Italy) there are supposedly fewer cases. [For general statistical data, agreeing in the main, see Lucke B. and Rea M. H.; J. A. M. A. 77, 935, 1921.—*Translator.*]

### Courses and Consequences of True Spontaneous Aneurysms

The smaller the artery, and the longer the dilated area, the longer, in point of time, the unchanged aneurysm has existed. Thus circoid aneurysms are often found in very old individuals. Saccular aneurysms are much more unfavorable, especially those with wide necks through which the dilating blood stream can enter. These are progressive; rupture is more imminent, the smaller the aneurysm. In boat-shaped, and narrownecked aneurysms, thrombosis quickly occurs, but rarely from stagnation; other factors, such as slowing of the stream in the dilated area and loss of endothelium, roughening on the inner surface of the sac, come into play. The former causes accumulation of leucocytes along the edges of the stream and whirlpools which fuse the platelets which, in turn cause cohesion of platelets and leucocytes to the wall. Fibrin is abundant in the thrombi. By successive deposit of layer on layer, the onion peel arrangement is brought about.

If the thrombus adjusts itself to the lumen of the vessel the result is favorable, but if it protrudes into the lumen, pieces may be torn loose and embolism result. Aneurysms of the popliteal artery are feared on account of the danger of gangrene, (comp. Haeller). The same may be said for ligation of this vessel, (see Hotz).

Occasionally a spontaneous, extensive organization occurs, and is equivalent to a cure. This is especially true if the thrombus continues in the artery itself and closes it to the next collateral, thus eliminating the aneurysm. If the collateral circulation will carry the blood past the thrombosed area, the same result is achieved as in the operative method of ligation above and below the aneurysm and splitting, cleaning and tamponade of the sac.

The large aneurysms of the arch and the thoracic part of the aorta with its ascending branches (Byloff), are of especial importance because of compression and encroachment on neighboring organs, both soft parts and bones. Partly by compression, and partly by erosion, the following organs are endangered: trachea, bronchi, lungs, pleura, pulmonary artery, pericardium, esophagus.

The aneurysm may rupture or perforate into any or several of these organs simultaneously. The author saw this in a 51 year old woman in whom a perforation into the esophagus as large as a silver half dollar was present, with another 3 cm. long × 1 cm. broad, into the left bronchus.

According to Baer, (lit.), only 15% of aneurysms of the aorta cause death by perforation.

Of the nerves endangered, the recurrent, especially the left, must be considered, since it encircles the arch, while the right encircles the right

subclavian artery. Compression of one causes paralysis of the vocal cord on the corresponding side, (cadaveric position). In unilateral paralysis, the voice loses its timber; bilateral paralysis results in aphony. Irritation of the fibres to the glottis causes spasm of the glottis. Perforations into the left auricle (lit. by Dahlen), the superior cava (lit. by Kieseritzky), and the pulmonary artery (lit. by Kappis, Hensen, Sternberg, Jankowich), are rare. The constant hammering of an aneurysm often destroys

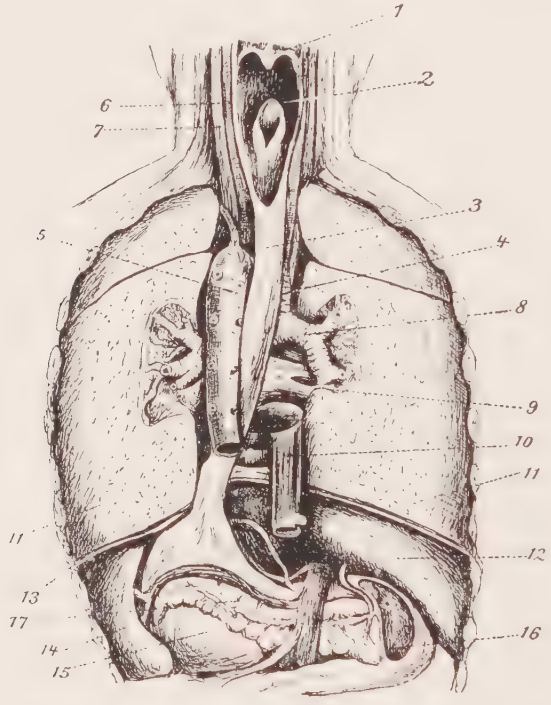



FIG. 82.—Position of viscera after removal of posterior body wall. This illustration is constructed on the basis of Fig. A, plate V of Rudinger, Topogr. Surg. Anatomy of Man. 1, soft palate with uvula; 2, entrance to larynx with epiglottis; 3, esophagus; 4, trachea extending on r. side somewhat above the esophagus; 5, arch of aorta and thoracic aorta; 6, common carotid lying along pharynx; 7, common jugular vein; 8, bifurcation of trachea into two bronchi, bronchi laid bare in hilum of lung; 9, pulmonary vein entering l. auricle; 10, inferior cava receiving the hepatic veins below the diaphragm; 11, both lungs; 12, posterior blunt margin of liver; 13, diaphragm lower on left than right; 14, spleen with vena lienalis running over the pancreas; 15, stomach; 16, duodenum opened posteriorly exposing duodenal surface of pylorus; 17, pancreas with its duct which unites at the duodenal concavity with the common duct which descends in a curve from above. The portal vein passes obliquely over the pancreas, incorporates the splenic vein and branches of the loops of the small bowel and runs in front of the inferior horizontal part of the duodenum upward behind the pancreas and stomach toward the hilum of the liver.

bone, *e.g.*, the vertebrae are soon eroded, but the cartilaginous disks and ligaments are more resistant. Pressure softening of the spinal cord itself is rare (Goldschmidt-Haas, lit.). The sternum and ribs are frequently perforated by erosion during which the wall of the sac including any adhe-

sions to surrounding parts, are also destroyed, with ultimate perforation. In this way also, false aneurysms bulge under the skin at the sternum or the ribs. In rare cases, perforation through the stretched skin occurs, but usually an extensive thrombosis within the sac protects against fatal hemorrhage.

The order of frequency in relation to the site of aneurysms of the aorta is as follows: the ascending aorta, as being mechanically the most actively used, is first. Koster adds as an explanation of this predilection, that this part to its enveloping fold of pericardium, derives its vasa vasorum from the coronary arteries which are frequently diseased. (Aneurysms of the sinus of Valsalva are rare, lit. by Blume.) Then follow in order of frequency: aneurysms of the arch, thoracic, and abdominal aorta. Thus, as a general rule, those of the aorta occur in places where the blood current strikes with especial force. These areas lie within a spiral line, which Rindfleisch called the breaker line; it begins anteriorly at the bulb of the aorta, and may be considered as gradually passing along toward the left, then backward, and downward to the posterior part of the descending aorta. Intrapericardial aneurysms situated at the bulb, push against the pulmonary artery, the right auricle and ventricle. Those located somewhat higher are directed forward against the sternum. Those in the ascending portion force themselves to the right against the right bronchus and lung. Adhesions or exudative pleuritis, and at times, perforation into the lungs, may result. If the breaker line is followed further, the aneurysms in the descending arch are directed against the trachea, pleural cavity, esophagus, recurrent nerve, bronchi, especially the left (Oliver-Cardarelli symptom: systolic down pull of the larynx), and more and more against the vertebral column and the posterior parts of the thorax, (comp. the topographic picture of the thoracic interior, fig. 82). Aneurysms in the lower part of the thorax, and especially of the abdominal aorta, are usually smaller, and infrequent, and apt to be latent clinically. Toward the periphery of a large aneurysm, the arterial pulse is delayed and weaker in comparison to the cardiac pulse. See details by Hofrichter as to aneurysms of the innominate which may be essentially intrathoracic or directed outward quite early.

### So-called Miliary Aneurysms (Fig. 13, P. 133.)

These occupy a separate place and are most frequently found in medium, small and smallest arteries. Only occasionally do they reach the size of lentils and peas; at other times they are almost microscopic. They are always multiple, frequently in large numbers. They are much more frequent in the brain than elsewhere (intestines—lungs), and occur mostly

in the central ganglia where they cause hemorrhages, (see under cerebral hemorrhage).

Those of the brain are spindle-shaped or globular, but sometimes saccular, (fig. 3, p. 133). They follow arteriosclerosis. According to recent investigations by Ellis (good illustrations), and Pick (lit.), these miliary aneurysms of the cerebral vessels are (*a*) dissecting aneurysms, because the blood escapes through a tear of the intima into the media or tunnels between media and adventitia, or (*b*) pseudo-aneurysms, blood sacs, *i.e.*, hematomas, communicating with the vessel lumen by a hole in the vessel wall and are bounded by fibrin, changed brain tissue, and illy defined elements of the ruptured vessel wall. These (*b*) develop either directly by rupture of an arteriosclerotic vessel, or from a primary dissecting aneurysm. In contradiction to earlier findings, Ellis and Pick could not demonstrate true aneurysms involving all layers, (see Unger). If rupture occurs, it is usually through several smaller or larger tears; if the wall of the sac is thick and its base (neck) is thin, the entire aneurysm may be completely torn off. For pseudo-dissecting aneurysms of small brain vessels, see p. 147.

### True Traumatic Aneurysms

A blunt external force (concussion, blow, fall) exerted on an otherwise perfectly healthy artery (especially the aorta), may be followed by circumscribed necrosis or tearing of the layers, especially of the media, and thus the vessel is weakened. An aneurysm forms at once by rupture, or the parietal lesion heals with functionally imperfect fibrous tissue, and the weakened area dilates secondarily (aneurysm cicatricium).

The author saw a saccular aneurysm as large as a walnut in the thoracic part of the otherwise perfectly healthy aorta of a sturdy young man. It had developed some months after a severe fall. The sequence of internal tearing, circumscribed necrosis, and fibrous cicatricial change of the vessel wall is easily understood in such cases, (see Moriani, D'Antona, Reichardt and E. Fraenkel). Traumatic aneurysms occur most frequently in the large peripheral arteries.

Malkoff's experiments, designed to produce aneurysms by trauma (crushing with clamps), were negative; the area either healed with narrowing, or rupture soon took place. Fabris succeeded in producing aneurysmal dilatation only after deep cauterization of the wall with silver nitrate, (see Nassetti).

Under this heading should also be included the cases discussed in the following chapter dealing with inner tearing of the aorta and other large arteries, which do not always lead to the formation of aneurysms, (see case of 18 year old male, p. 144).

## So-called Dissecting Aneurysms

These develop when the fatty degenerated intima or both the intima and the media tear, even over the smallest space. The blood tunnels between the layers of the wall, separating them by an intramural hematoma. The tunneling occurs between intima and muscularis, or, more usually, between the outer layers of the media, and between muscularis and adventitia. In form, a saccular circumscribed is differentiated from a cylindrical diffuse type, (p. 133 illustr. 4, 12 and figs. 83 and 84). The most important dissecting aneurysm is that following rupture of the aorta.

**Formation.**—The tear occurs in arteriosclerosis from overdistension of the intima or from perforation of an atheromatous focus. It is infrequent in atrophy of the elastic tissue of a senile aorta without marked changes of the intima, (Bay, lit.). When there is no arteriosclerosis, it occurs usually in youthful individuals, *e.g.*, in a boy 14 years old (Lilienfeld), and in one, 15 years old (Huebachmann), from factors such as trauma, abnormal increase in blood pressure, etc., which injure a perfectly smooth inner layer even when no fatty degeneration is apparent. Sometimes the vessel is of particularly delicate structure, the media is less elastic and firm, but even an apparently quite perfect aorta tears. In Busse's case, the aorta was 10 cm. in diameter and the heart markedly hypertrophic; in E. Hoffmann's case, the aorta was wide, but microscopically normal, (see also Oppenheim). Under trauma, we must include such factors as direct blunt force which indeed may injure the inner without affecting the outer layers. A sudden rise of blood pressure such as occurs from lifting a heavy burden, etc., (see Jenner), or from emotional excitement or terror (*e.g.*, Hart's case), may be responsible for these so-called spontaneous ruptures of the aorta. For example, in a young, delicate woman, the author found an internal rupture of the abdominal aorta, which showed only slight fatty degeneration of the intima, thus giving no demonstrable excuse for the rupture. Perhaps it was abdominal compression during defecation or trauma (?). The intima showed a circular tear and was separated from the outer layers as far as the iliacs; perforation followed through muscularis and adventitia which had undergone aneurysmal bulging; the blood flowed into the retroperitoneal cellular tissue, and the peritoneum was tunneled by massive hemorrhage and forced upward in the right lateral abdominal region by a tumor-like extravasation the size of a man's head. Death resulted from internal exsanguination. In another case, (33 year old woman), the illness of 10 weeks duration ended in sudden death with dyspnea during a labor pain. Here the "trauma" was increase of blood pressure during labor, followed by delirium cordis. At autopsy, the aorta was 8 cm. in diameter and torn

transversely 1 cm. above the valves through the delicate intima, thus exposing the media. Thrombosis occurred with embolism into the right internal carotid artery. Wegelin saw bilateral dissecting aneurysms in the thyroid artery in eclampsia, with separation between media and adventitia; the cause was probably increase of blood pressure during a convulsion. Cases have been reported in which the torn aorta was dilated, or in which there was hypertrophy of the left ventricle (Schede, lit.) and general arteriosclerosis with contracted kidney as the causative factors, (see Loffler). Stenosis of the isthmus, (see p. 93), even if of but slight degree (Oppenheim) favors the development of aortic rupture, (lit. by Sella, see P. Frankel, Binder). Babes and Mironescu, also Moriani (lit.), report

FIG. 83.—Dissecting aneurysm of an iliac artery filled with thrombotic mass. The opening in the intima which leads into the intraparietal sac is not shown; 9/10 nat. size.

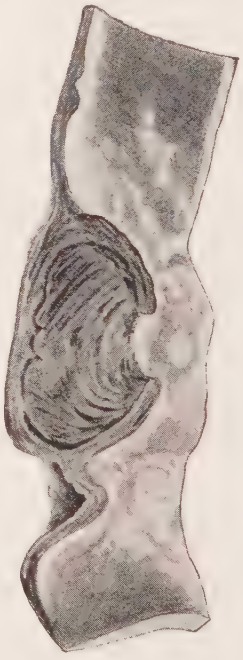


FIG. 84.—Humpy projecting dissecting aneurysm of the abdominal aorta, filled with thrombi; arteriosclerosis, 76 year old man; longitudinal section; 9/10 nat. size.

cases in which there were inflammatory or degenerative changes in the media; thus a non-dissecting arteritis may be the primary cause by allowing the formation of intramural hematomas (see D'Antona). E. Krunkenberg reasons that the intramural blood mass may have come from the vasa vasorum. As Benda and Fleckemann emphasize (see also Bay), a healthy media offers much greater resistance to separation of its layers than one diseased. For instance, in a strong 18 year old boy, whose abdomen had been crushed, the author saw a wide open tear in the right common iliac artery with no dissection. Thrombosis on the ruptured intima, embolism into the posterior tibial artery, and gangrene of the right lower leg followed, (see illustr. of this case by Hildebrand).

The aorta tears most frequently in its intrapericardial portion, then in its arch. The typical tear, situated about the width of a finger above the valves, (*i.e.*, on the level of the invaginating vincula which encloses the aorta and pulmonary artery), is caused, according to some, by the pull exerted at the point of insertion of the valves, but according to Rindfleisch, it is systolic. Alongside the vinculum of the ascending limb, rarely of the descending, the course is transverse, frequently almost circular, but may be cornered or hooked. Occasionally, especially in atheromatosis, longitudinal tears occur (rupture tears). Rupture of the more resistant outer layers of the aneurysm leads to hemopericardium. Dissecting aneurysm of the pulmonary artery is rare. (See Durno's case with rupture into the pericardium.) Thrombosis occurs quite readily in a saccular dissecting aneurysm—figs. 83 and 84.

Cylindrical dissecting aneurysms (fig. 12, p. 133) in which the internal site of rupture is often located in the ascending aorta, may continue far toward the periphery, and more or less completely split the aorta and its larger branches, down to the popliteal, and up to the carotids. Thus there is a blood-filled casing around an inner tube, the old channel, or perhaps a double tube (see b. fig. 85). The branches, whether dissected or not, remain in continuity with the inner tube, or tear circularly near their openings (s. fig. 85, d) and only their stumps remain on the isolated inner tube. The distal main part of the arterial branch which may be dissected or not, must therefore be supplied with blood from the outer tube. Blood entering through the primary tear may circulate between the separated layers of the media, or of the intima and media, as the case may be, as if in a second, (outer) tube; if it breaks through the media, predisposed by atheromatosis, it may leave the false channel and reenter its old (inner) tube, (back perforation). Generally, the adventitia of the aneurysm tears. If this secondary rupture occurs within the pericardium, hemopericardium results, but death is often delayed a few hours. Dissecting aneurysms also perforate into the pleural cavity or lung, as in a 75 year old man with a dissecting aneurysm of the thoracic aorta; death resulted from exsanguination or asphyxia. In another intrapericardial dissecting aneurysm of the aorta, the almost circular rupture of the ascending limb occurred suddenly during work in a 59 year old man. The blood forced itself alongside of the branches of the pulmonary arteries into the alveoli of the lung; the patient had hemoptysis and died at the end of the first day. The pericardium contained 700 cc. of blood, (see c.f. Schw. No. 10, 1906). If a dissecting aneurysm of the aorta tears numerous intercostal arteries with subsequent occlusion, the nutrition of the spinal cord, otherwise supplied only by the vertebral arteries, may be endangered, and paraplegia follow, (Reitter, lit.). The intraparietal sac may become

smooth and lined with a sort of intima covered by endothelium (Bostroem, lit.), which is considered a form of cure, (Harbitz, Borger, Schede, lit., MacCallum, Vorpahl, E. Schmidt, lit., Hart; fig. 85). This occurs espe-

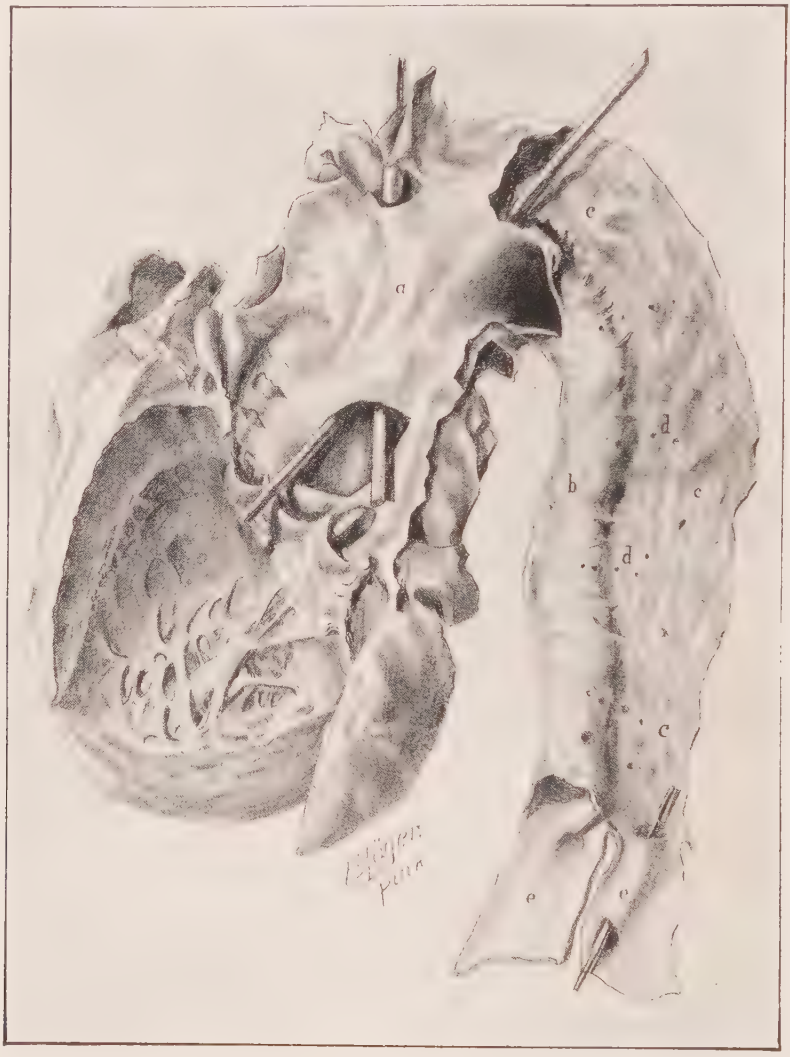



FIG. 85.—Dissecting aneurysm of the aorta (from Busse, V. A. 183, 1906); a, inner surface of aorta with tear in ascending part; b, posterior surface of the unopened descending and abdominal aorta (old tube lying on right side) also forming anterior wall of the opened new tube formed by dissection; c, inner surface of the new (aneurysmal) tube, lined with newly formed membrane; d, openings of the intercostal arteries; e, inner surface of the common iliac arteries; here the new tube opens, passing into the old bed through a slit-like opening.

cially if the blood in the aneurysm forces its way back into the old channel as in the so-called chronic aneurysms in contradistinction to acute external

perforations which are always fatal. In rare cases, dissecting aneurysms heal by adhesions and the primary rupture is closed by scar tissue (v. Moller). Even ruptures of the inner coats of the beginning of the aorta, if they do not lead to completely developed dissecting aneurysms, sometimes heal leaving a furrow or gap, (healed rupture of aorta). But the cicatricial area is later bulged to an aneurysm, (secondary true aneurysm). Every museum, the museum at Basle included, possesses such preparations. For interesting cases of this kind with insufficiency of the valves of the aorta, including lit., see Heller, Ernst, Asahi Busse; in reference to spontaneous and traumatic rupture of the aorta, see P. Franckel, Rossle, Berblinger, Jenner. Chiari and Maresch saw sudden death follow inversion of the inner cylinder of a dissecting aneurysm of the ascending limb of the aorta in which the detached intima rolled up in a wad and plugged the outlet of the large vessels, thus blocking the blood supply to the brain.

A picture somewhat similar to that of dissecting aneurysm is produced when the perivascular lymph sheaths of the small cerebral vessels become filled with blood, (spurious dissecting aneurysm). This is not an aneurysm, only an escape of blood into lymph spaces already formed, (fig. 8, p. 133). It must be added, however, that true dissecting aneurysms frequently occur in the small cerebral vessels, (see p. 141).

### Embolic Aneurysm

According to Ponfick, simple embolic aneurysms develop when emboli of hard, pointed, calcified particles detached from valves or thrombi, penetrate the wall of some small arterial branch, or produce pressure necrosis. In both cases the resistance of the wall is lost. In comparison to mycotic aneurysms, these forms are certainly rare, and are most frequent in the basal arteries of the brain. Their rupture causes quickly fatal, intracranial hemorrhages (subdural and intrameningeal). A similar process in horses is found, especially in the mesenteric arteries, as the so-called worm aneurysms, caused by a parasite—strongilus armatus which enters the vessels and causes the necessary parietal changes.

Mycotic or infectious embolic aneurysms (rare), according to Eppinger, are caused by infected emboli originating in mycotic acute ulcerative endocarditis of the left heart. The emboli are usually stopped at a branch (sup. mesenteric, basal cerebral, especially the thoracic, femoral, etc., Unger, lit.). Acute ulcerative processes begin in the intima, the wall eventually bulges and an aneurysm forms containing a thrombus laden with bacteria, (lit. by Hamburger; p. 123).

If the infectious material does not occlude a vessel (like an embolus), but is merely adherent to the intima, it may be spoken of as a metastatic, mycotic aneurysm, (comp. p. 122).

### Erosion Aneurysm. Ulceration Aneurysm

Two forms are differentiated: ulceration from without or from within.

These develop as follows: pus from a wound, or any focus, especially tuberculous granulations in a pulmonary cavity, or gastric ulcers, meets the adventitia of an artery; *i.e.*, a periarteritis beginning at a circumscribed area, infiltrates the wall which becomes necrotic and softened; as fibrosis occurs, bulging increases, (true aneurysm), or rupture by erosion takes place quite early.

If the outer coats are destroyed at any circumscribed area and the inner coats push outward, it is called a hernial aneurysm.

A pseudo aneurysm may also form, even in the aorta; Foa described such a case in which the erosion started from suppurating lymph nodes. Rosner saw fatal rupture of an aneurysm of the ascending aorta caused by a mediastinal abscess due to a typhoid complication.

In pulmonary cavities, aneurysmal dilatations are frequent, (fig. 15, p. 133) usually the size of pinheads to peas, rarely as large as beans, (see figs. 201 and 202). The wall consists only of bulging thrombotic material (platelets and fibrin, compare spurious traumatic aneurysm, p. 132; see histology of Menetrier, Milano). If rupture occurs, hemoptysis follows, because the cavity communicates with a bronchus. According to Fraentzels investigations in the Charite in Berlin, aneurysms are found in 75% of all fatal pulmonary hemorrhages in phthisis. Aneurysms may be observed in bronchiectasias, and occasionally in actinomycosis, (Reiche; see p. 132).

A mycotic aneurysm springing from the ulcerated intima, apart from embolic aneurysms (see p. 147), *e.g.*, of the ascending aorta, may develop by continuity or contact infection from an ulcerative aortic endocarditis (see purulent arteritis p. 122), and may also involve the sinus of Valsalva or other areas near the valves, (see Stolting, lit.).

Since the wall of the aorta at its beginning receives vasa vasorum from the coronary arteries, we must think of mycotic embolic aneurysms in this region beginning in the outer parietal layers, (comp. Gambaroff, McCrae, Klotz, lit., Kloss).

Metastatic deposits of infectious material from distant areas on the inner surface of the aorta are rare, especially when followed by the formation of aneurysms (metastatic—not embolic aneurysms), see Vanzetti, lit., p. 123, and Koritschoner, Edenhuizen, lit.

### Arterio-venous Aneurysms

(*a*) **Aneurysmal Varix.**—Injury to both an artery and adjacent vein as during the use of the spring knife in phlebotomy on the median vein

and the brachial artery, may allow arterial blood to enter a vein, distend it locally, or cause it to pulsate over longer distances.

Simple arterio-venous fistula without the formation of varices does not belong in this discussion.

(*b*) Intermediate varicose aneurysm; more exactly intermediate saccular varicose aneurysm, (Broca). When an artery and an adjacent vein

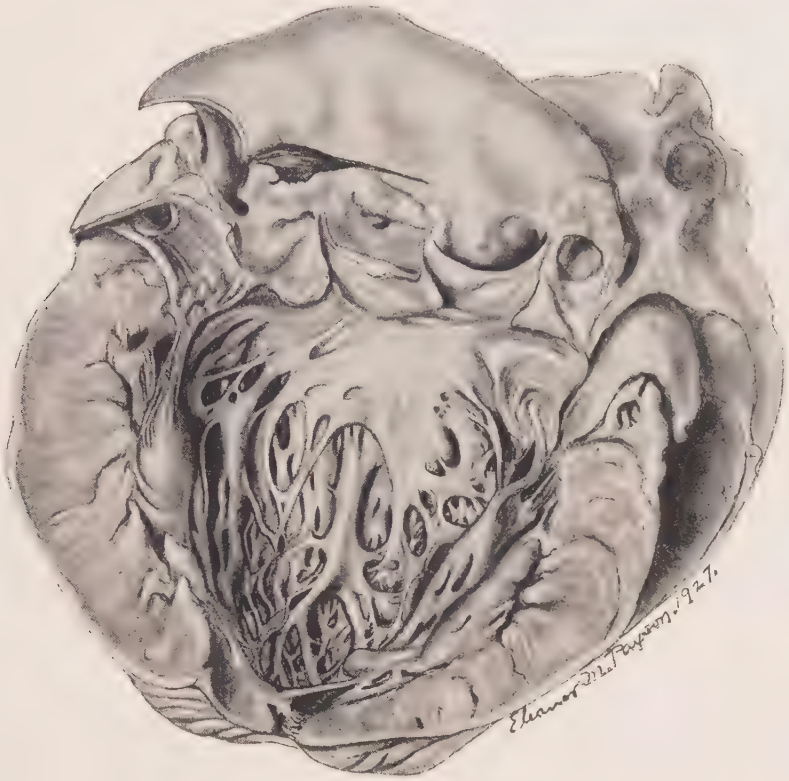


FIG. 86.—Transverse rupture of the aorta just above the aortic valve from a woman 40 years old who complained of sudden, intense, precordial pain following what seemed to be a mild exertion. Attention was directed to the heart by the pain, dyspnea, irregular pulse, increased area of dullness and muffled sounds but the diagnosis was not established until autopsy 36 hours later. Such cases are baffling from the pathological, physiological viewpoint, but they occur often enough to be a possibility acceptable in clinical diagnosis. Gross and histological examination showed no lesions in the aorta except the tear.

are both injured at the same time, a false aneurysm is formed between artery and vein by an intermediary pulsating sac which carries the blood from the artery to the vein; the latter may become varicose and dilated by the abnormal blood pressure (p. 133).

(*c*) Arterio-venous aneurysms in a narrower sense are caused when a true aneurysm perforates into a vein, *e.g.*, from the aorta into the pulmonary vein, or from the ascending aorta into the superior vena cava.

We may also designate (*a*) as an arterio-venous aneurysm with a venous sac, (*b*) with a false sac, (*c*) with an arterial sac.

In (*a*) the vein, and in (*b*) and (*c*) the artery plays the greater part in the sac formation. According to Kuttner, pseudo aneurysms may be simulated by the bruit of a hidden true arterio-venous aneurysm, when for anatomical reasons it is conducted over a long distance and is more plainly perceived at some distant place than at its real location.

**Translator's Remarks.**—The effects of short-circuiting blood from an artery to a vein whether through an aneurysm or a simple fistula are quite pronounced and manifested directly or indirectly on all parts of the body. In general, they depend on the size of the communications, *i.e.*, the amount of blood passing through. The changes occurring immediately after a fistula is opened are a fall in arterial blood pressure, increased heart rate, increased venous pressure. The first is gradually compensated by an increase in the total blood volume, the heart rate decreases, but the heart action remains more vigorous and the organ hypertrophies, the systolic blood pressure rises to its previous level or higher, the diastolic pressure is low, the pulse pressure is increased and the venous pressure high. When the hypertrophied heart fails, the signs of chronic passive congestion are manifested in all organs. In general such aneurysms or fistulae tend to increase in size, although healing of a small fistula is possible. There is increasing dilatation of both the artery and vein involved. See Holman E., Kolls A. C.; Arch. Surg. 9, 822–879, 1924; and Holman E. Ann. Surg. 801, 1924.

### CONGENITAL ANEURYSMS (RARE)

Occasionally one occurs at the duct of Botalli (see fig. 41, p. 97), and also in the abdominal aorta. Lexer saw a fusiform congenital aneurysm of the brachial artery in a child 1 year old.

### TRUE DIFFUSE PHLEBARTERIECTASIS

According to Lawen, this is an infrequent, progressive dilatation of one arterial area including capillaries and efferent veins without the formation of new vessels, probably congenital in its beginning, and occurring chiefly in the upper extremities (O. Weber). The extremity may lengthen (Ebstein lit.).

## Hypoplasia and Atrophy

See p. 72 in reference to hypoplasia of the aorta (narrow aorta). It is described by v. Wiesner in status thymo-lymphaticus; Binswanger and Schaxel report it in cerebral arteries in various psychic disturbances, (Orliansky),—also in suicides, and as the cause of cerebral hemorrhages

in eclampsia. The hypoplasia affects especially the elastic and muscular elements. Atrophy is seen physiologically when Botalli's duct, and the umbilical arteries disappear (see p. 96 and 117), as well as in the involution of the vessels of the gravid uterus. It is seen in the elastica and musculature in advancing age, and often in the media in arteriosclerosis, secondary to intima sclerosis (see p. 111).

### Hypertrophy and Hyperplasia

**Hypertrophy** is physiological during adolescence, also in the uterine arteries during pregnancy, especially in the media, while during puerperal involution the vessels undergo atrophy. Atrophy of musculature via fatty degeneration and hyalin metamorphosis, and a real new formation of the vessel wall take place within the old vessel lumena (see details by Goodall). We see functional hypertrophy of the muscularis in increased pressure in the arterial system. It represents an analogy to cardiac hypertrophy from labor, and like this, results frequently in chronic nephritis. Hypertrophy is always accompanied by thickening of the intima. Vicarious hypertrophy with dilatation and a certain amount of new vessel formation develop if collateral channels must assume new work, *e.g.*, in the artery of the healthy kidney when the other is completely atrophic (comp. collateral tracts in stenosis of the isthmus, p. 93). If a large tumor grows in an organ and makes great demands for nutrition, not only hypertrophy, but actual hyperplasia, *i.e.*, formation of new vessels, takes place. In circoid aneurysms, dilatation and lengthening is seen with thickening of the wall. If the musculature degenerates, the wall later becomes atrophic and thin.

**New Formations Consisting of Vessels.**—It is necessary to differentiate between the circoid or serpentine aneurysm and the racemose arterial angioma (lit. Sonntag), in contradistinction to the venous, which has been described as involving fingers, hand and foot.. It is a new formation of vessels in which the convolutions and dilatations of one or several neighboring arteries are continued into the branches, indeed to the capillaries and even to the veins. Those chiefly taking part are the arteries of the scalp (lit. O. Schmitt), of the face, and of the arm (hand and forearm); it rarely invades the meningeal vessels, but in Blank's case the artery of the fissure of Sylvius was affected. Pulsation and bruit have been observed. Telangiectasias belong to the angiomas, or vessel tumors, and are progressive new formations of numerous vessels with eventual dilatation, which grow in the skin as vascular naevi and manifest themselves as flat red blotches or warty prominences (see under skin). Cavernous angiomas consist of wide blood spaces lined with endothelium and show numerous intercommunications.

Tumors starting from the arterial wall have been described in but few isolated cases. Auffermann (lit.) speaks of sarcomas of the aorta with peculiar giant cells, but these tumors are of debatable genesis. The growth of primary tumors from vessel sheaths is also doubtful (Langenbeck); they have been described as lipomas, fibromas, myxomas, sarcomas, mostly of the carotids and femorals. Lately Ferrarini (lit.) supported the belief of their existence.

## VEINS

### Thrombosis and Embolism

Thrombosis is a term meaning coagulation—the formation of plugs (thrombi) within the blood vessels consisting of substances derived from the blood. Quite frequently they may completely or partially close the lumen, or be transported as emboli.

Thrombosis plays such an important part in diseases of the veins that a short resumé of this theme will be given, although it really belongs to general pathological anatomy. We speak of tumor thrombi if vessels are more or less completely plugged by tumor masses (see p. 167), also of tuberculous thrombi (see p. 159), and of gummatous thrombi (see p. 159), in contradistinction to "simple thrombi."

**Difference in Thrombi According to Composition and Origin.**—Coagulation thrombi are formed by the precipitation and cohesion of blood elements. We may have pure platelet thrombi, or, if the percentage of leucocytes is high, leucocytic thrombi, having also a percentage of fibrin. Coagulation thrombi may be similar to blood clots, but they often contain a quantity of "deposit" material, usually platelet thrombi, which start the coagulation thrombosis (Kusama), and for this reason are spoken of as combined thrombi. Pure coagulation thrombi are seen after transfusion of foreign blood, etc.

According to their external appearance they are differentiated as red, white, or gray and mixed thrombi. The red correspond to coagulation thrombi, the white and gray are precipitation thrombi. The mixed are a combination of both, and are, like precipitation thrombi, often plainly laminated with alternating white and red layers. Their further growth is possible only in flowing blood, like all true precipitation thrombi. In other cases, a coagulation thrombus forms a thick coating around a precipitation thrombus. Hyalin thrombi are either precipitation thrombi rich in fibrin which have undergone homogeneous transformation (white), or consist of agglutinated erythrocytes (red).

**Factors Favoring the Formation of Thrombi in the Veins.**—Changes in the walls consisting of loss of endothelium and severe injury from

phlebitis favor separation of substances from the blood stream, especially platelets.

Changes in the flow of blood; (*a*) cessation or stagnation of flow of blood; but to cause stagnation or coagulation thrombosis, a parietal lesion or an alteration of the blood is necessary. (*b*) Slowing is an essential factor in dilatation of the vessels by varices and aneurysms—dilatation thrombosis takes place. (*c*) Congestion. (*d*) Diminished cardiac power (marantic thrombosis); thrombosis, as a rule, commences with precipitation and this may be succeeded by coagulation—often to a wide extent.

A third factor in the formation of thrombi consists of changes in the condition of the blood, such as, increase of platelets with their increased viscosity (as in chlorosis), injury to blood by infection which favors primary precipitation and secondary coagulation, transfusion of foreign blood, causing pure coagulation thrombosis, and fermentation thrombosis, thermic injury, etc.

### Location of Thrombi

They may be parietal (fig. 88); on the valve leaflets (fig. 87), especially in the pockets, because the current of blood favors the formation of eddies,

FIG. 87.—Thrombus with rifled surface resting on a valve of the right crural vein in typhoid fever; man 35 years old; ½ nat. size.

FIG. 88.—Parietal thrombus of the aorta almost occluding the lumen of the sup. mesent. artery; woman 55 years old with pulmonary phthisis.

(see v. Recklinghausen). Obstructing thrombi are to be differentiated. These latter may have their origin in the other two; their rough surfaces favor new deposits which are arranged concentrically, or they may develop because the growth of the thrombi leads to blocking of the vessels and

stagnation (stagnation thrombi), on the other side of the occlusion. The first two types are frequently found in the veins of the lower extremities, especially in the saphenous vein; the obstructing thrombi are often in the dural sinus, the pudendal plexus, uterus, etc. We may also differentiate between autochthonous (formed at the place where located) and those carried to the next large branch.

### Metamorphosis of Thrombi

The color of the red thrombus changes in time to rusty brown, finally to a light brown, from partly granular, and partly crystalline pigment. The thrombus shrinks, dries and becomes harder. But it may soften, and a red or brownish red opaque mush result from a red thrombus.

Fig. 89.—Cavernous metamorphosis of the left common iliac vein and the hypogastric vein; in the crural vein a cylindrical old adherent thrombus (partly cut open), 21 year old factory girl with caseous pneumonia; 5/6 natural size.

The differentiations made are: puriform softening, changing into a pus-like molecular mush (comp. p. 79 under heart); purulent softening, true pus caused by infections (septic thrombi), ichorous softening caused by ichorous infection, in which the thrombus becomes almost fluid and dirty brown to greenish black in color. Infectious thrombi may be caused by phlebitis, and in their turn may cause it, (see phlebitis pp. 157–158).

If a thrombus fuses with the wall of the vein, it is spoken of as organization of the thrombus and represents nothing else than a productive inflammation of the venous wall (productive thrombophlebitis) in which the thrombotic masses remain quite passive. The integrity of the wall is essential for organization, and to progress satisfactorily it must not be exposed to infection. Otherwise it develops exactly as in arteries. First the periphery of the thrombus is involved, and intima and the connective tissue elements of the deepest layers of the media produce cells which, with vessels from the media, penetrate into the thrombus. Then an interstitial substance appears between the proliferating cells and later becomes thready, fibrous and poorer in cells, but still contains brown pigment granules.

Small thrombosed veins may change to solid cicatricial cords; larger ones at times may become patulous (recanalization, see p. 120). The author

made a drawing from a preparation in Basle which is a pronounced example of this process, (fig. 89).

Thrombi may also dry and become petrified by impregnation with lime salts. This is seen in motile white thrombi in the sacs of varicose veins; they are calcified, and become globular from rotation. They may become adherent secondarily (see Wydler). Ribbert thinks that phleboliths are principally thrombi formed by concentric fibrin precipitations which organize and calcify afterwards. Not rarely, phleboliths are partially ossified, (Wydler). They are most frequent in the veins of the spleen, in the broad ligament of the adult female, and in the prostatic plexus, in which they occur quite frequently, even in early life. They are found also in the veins of the bladder, quite rarely of the rectum. Phleboliths are unusual in phlebectasias of the venae minimal in the cardiac auricular septum (the right), and at the lower lateral edge of the foramen ovale, (lit. by Geipel, Escher, Weber, Frank). The author saw such a case in a woman 31 years old with a phlebolith the size of a lentil in the vermiform veins, (comp. cases of Bostroem, Rau). In a man 78 years old in whom there was a varix the size of a large bean filled with a lamellated red thrombus, phleboliths were absent.

### Consequences of Thrombosis (see also p. 158)

Thrombosis often has important consequences. These may be local disturbances of nutrition or inflammations, *e.g.*, red softening of the brain in extensive non-infective sinus thrombosis; meningitis or brain abscess if infection accompanies it, etc., or embolism. For consequences in the latter cases it is essential to know whether they are from non-infected, or infected thrombi.

The term "emboli" is used of all bodies, including bullets, etc., (see Jaffe, Borst), which are carried along in the blood stream, and have a tendency to become wedged in a vessel lumen, (see chapter on embolism, under lung).

Non-infectious venous thrombi, *e.g.*, in the femoral vein in typhoid, (see fig. 87), or in varices, can, if large enough, acutely close the trunk of the pulmonary artery causing death, (see under lungs). If small, they occlude a branch, most frequently one of the pulmonary artery into which they are carried, and cause local nutritional disturbances with anemic and hemorrhagic infarction. Embolism has no effect if the embolus rides on a vessel bifurcation without causing closure of lumen, or if collateral branches come to the rescue as soon as occlusion occurs.

In infectious embolism the story is different, since they originate from softened septic thrombi. Multiple embolic and metastatic abscesses and infectious foci appear in pyemia. In this case also, the pulmonary

artery often stops the larger emboli. But they are also disseminated in the greater circulation and cause abscess formation everywhere. Infectious thrombophlebitis of the uterine veins, sometimes a sequel of abortion or parturition, and infected wounds, furnished grounds for Cruveilhier's dictum: "Phlebitis dominates the whole of pathology," and later Virchow wrote his classic works on thrombosis and embolism which supplied much material to pathological anatomy. With progression in antisepsis, pyemia has become rarer.

### Inflammation of Veins, Phlebitis

The structure of veins is essentially analogous to that of arteries, but the media is smaller and all the elements are weaker, although they are arranged, especially the elastic fibres, with more exactness, and the layers are more closely united than in arteries. For this reason, in parietal inflammation, no plain separation appears into endo-, meso-, and periphlebitis. An important distinction between veins and arteries is the reaction of the smallest twigs in tissue inflammation; arteries do not show perceptible anatomical lesions while the veins show peripheral grouping of leucocytes, and as in capillaries, leucocytic diapedesis through the wall has been demonstrated clinically and experimentally, particularly by Cohnheim. Several forms of phlebitis can be distinguished:

**Productive Phlebitis.**—This is also called adhesive or organizing, because the inflammatory proliferation grows through the thrombus and holds it firm. This takes place in connection with thrombosis either from within (see p. 154, organization of thrombus), or from without, from an inflammatory process in the neighborhood (periphlebitis).

Chronic productive phlebitis causes thickening of all the layers (hyperplastic chronic phlebitis), fibrous-hyalin metamorphosis with atrophy of elastic fibres, irregularity in shape, narrowing of the lumen (fig. 90), and, occasionally, obliteration. This is frequent in the saphenous vein and is also called phlebosclerosis (see Barach).

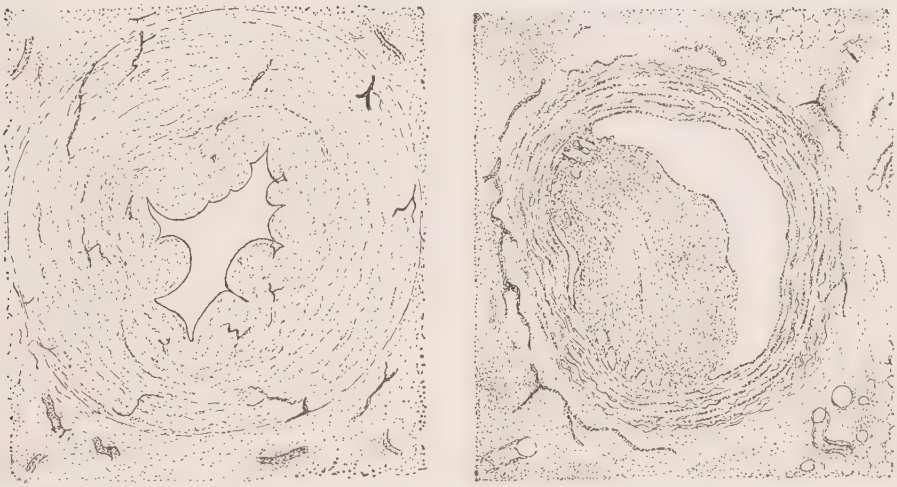
In chronic hyperplastic phlebitis, the muscle fibres may also participate in the general proliferation; they can be seen deviating in an arch to enter the thickened intima as, *e.g.*, in lupous tissue (see Wallart).

**Infectious Phlebitis (Thrombophlebitis).**—Pathogenic organisms attack the venous wall from without or from within. Their effect varies, and we differentiate between milder forms—simple exudative phlebitis—and the more severe suppurative and gangrenous varieties.

Thrombosis is combined with phlebitis with exceptional frequency as thrombophlebitis, or better, "phlebitic thrombosis."

If phlebitis is the start, and inflammation enters the wall, there is first marked hyperemia of vessels, exudate passes from them into the

lymph spaces of the wall which now appears very cellular because of the proliferating endothelium of the lymph spaces; there is then an increase of lymphocytes and migrating polymorphonuclear leucocytes. The exudate may be fluid with abundant cells and albumen, or may assume a purulent character, in which case the wall is filled with leucocytes. If a suppurative periphlebitis is transmitted to the venous wall the inflammation sometimes progresses for a distance along the vessel, since the connective tissue sheath of the veins is quite resistant, and thus new abscesses arise in the vicinity.



A B

FIGS. 90–91.—A Chronic hyperplastic phlebitis (phlebosclerosis) of the saphenous vein with crural ulcer. B So-called thrombophlebitis, better phlebitic thrombosis of an arm vein in erysipelas (see text) (both low power).

The vein is surrounded by a purulent coat, becomes isolated from its surroundings, and undergoes necrosis.

When the adventitia is penetrated the other layers are promptly involved. The wall becomes thick, yellow, or red spotted according to whether purulent infiltration or hemorrhages from hyperemic parietal vessels have occurred. The wall may be ten times its normal thickness, and does not collapse on section. The meshes of its elastic lamellae are widened, the fibres partly destroyed, the muscle cells swollen, the layers loosened and dissected (phlebitis dissecans).

Koster has shown that the lymph channels which he demonstrated in the venous wall, conduct the inflammation further, so that phlebitis is also a lymphangitis. It is also the lymph channels which carry the infection upward alongside the veins, as mentioned above.

This close relationship between lymph vessels and veins is observed, for instance, in infected wounds of the extremities, as in the removal of a

corn without antiseptic precautions. There first appear smooth brownish red striations as signs of lymphangitis; when phlebitis sets in, there are dark blue, thick strands which harden after thrombosis. As soon as the wall is attacked by infection, an exudate passing from the wall spreads over the intima and is followed by thrombosis. (This was called pseudomembranous phlebitis by Hunter; see Orth and Schum: exudative phlebitis.)

Inflammatory exudation is made possible to the inner surface through the vasa vasorum (Koster, Ebeling), as in serous membranes. Leucocytes reach the lumen from the wall and contribute to the formation of the thrombus, which, in addition to these, consists of other blood elements such as platelets and erythrocytes.

As infection progresses, the thrombus becomes green and contains pyogenic organisms in great numbers. The inner layers of the intima are necrotic, and the cells lose their power of nuclear staining.

On account of the constant combination of thrombosis and phlebitis, it is often called thrombophlebitis instead of infectious phlebitis, but "phlebitic thrombosis" is a more exact term, as mentioned above.

The process is somewhat reversed if the causes of inflammation are primarily within the lumen of the vein and thus start a primary infectious thrombosis. This process is the more common, and is also called thrombophlebitis. Microorganisms penetrate the intima causing its necrosis just as in ulcerative endocarditis. Active exudation and cellular infiltration from the vasa vasorum take place around the necrosis; the wall is thickened by fluid and pus cells which undergo disintegration (suppurative phlebitis). In gangrenous phlebitis, the wall is putrified, spongy, friable, cracked and discolored. On the intima are deposited yellow or green pseudomembranous fibrin coatings admixed with leucocytes derived from the wall. Thrombi rich in leucocytes and organisms may be superimposed.

Septic thrombi from purulent or putrefactive disintegration are the source of embolic abscesses, especially in the lungs, and of general pyemia (see p. 157).

The veins most frequently attacked by thrombophlebitis are: (*a*) saphenous vein in leg ulcer (see under varices, p. 166), (*b*) uterine veins following infection of the uterine wall, as after separation of the placenta, when many veins are wide open.

Thrombophlebitis may extend to the spermatic veins, the hypogastrics, and even the inferior cava and the femoral veins, the latter producing phlegmasia alba dolens (see under puerperal fever).

(*c*) Hemorrhoidal and vesical veins (see under hemorrhoids, p. 165).

(*d*) Umbilical vein of the new born (see under liver).

(*e*) Veins of the diploe (valveless, with many communications with those of the inner and the outer surfaces of the skull), and the dural sinus

with the internal jugular. Thrombophlebitis and meningitis or brain abscess may follow infected skull wounds, especially in the purulent and necrotic processes of the petrous portion of the temporal bone. There is also danger to the sigmoid sinus, and later, the internal jugular following otitis media (see under brain).

(*f*) The portal vein and its roots (see appendicitis and pyelophlebitis under liver).

(*g*) Veins of the bone marrow in osteomyelitis (see under bone). For thrombophlebitis migrans of peripheral veins, see pp. 121, 160 and 168.

### Specific Inflammations.

**Tuberculosis.**—Tubercles of the intima of veins, especially those of the lungs, are of great importance. They develop when tubercle bacilli enter the intima from the blood (tuberculous endophlebitis), or when tuberculous processes in the neighborhood extend to the wall of the vein (tuberculous periphlebitis). If the latter spread to the intima, they produce plateaus or polypoid excrescences called tuberculous thrombi and have common thrombi superimposed (tuberculous thrombophlebitis; see under miliary tuberculosis of lungs).

When a tuberculous formation softens and tubercle bacilli are liberated into the blood more or less regularly, or suddenly—this has frequently been demonstrated during life,—a subacute or acute general miliary tuberculosis results (Weigert).

Intima tubercles, not disintegrated, or encapsulated by connective tissue proliferation of the intima, or in superimposed thrombi, are harmless. The rupture of large tuberculous foci into veins is rare. The author saw miliary tuberculosis follow the rupture over 1 cm. in breadth of a softened cervical lymph nodule which had bulged into the right interior jugular vein of a woman 26 years of age.

In a second case, (man 21 years of age), a caseous nodule larger than a pea, with an ulcerated surface, attached to the wall of a softened caseous lymph node, containing a cavity the size of a cherry and attached posteriorly to the vein bulged into the lumen of the left internal jugular vein. (See Will for rupture into the superior vena cava.)

Syphilis of veins is of very little importance compared to arterial syphilis.

In the syphilitic newborn it may occasionally be important in inflammation of the vein, (cellular infiltration and edema), also in the arteries of the funis (see there).

More frequently, phlebitis and periphlebitis can be found in specifically diseased organs such as the liver (see there). Gummatous changes in

large veins are rare (Stocklin); there may be gummatous thrombosis or gummatous periphlebitis with non-specific secondary productive thrombophlebitis and obliteration (A. Frankel, Pawel, Benda). Chiari presupposes a syphilitic origin for the cases of fatal independent endophlebitis obliterans of the main trunks of the hepatic vein described by him. Simmonds assumes the same etiology in sclerosis of the portal vein.

According to Rieder's investigations, among the various results of syphilis, there may be marked venous changes such as peri-, meso-, and endophlebitis, partly cellular, partly fibrous with lymphangitis, even in hard chancre; the same is true of syphilitic rectal stricture. On the other hand, endarteritis may recede (comp. Abramow). According to Hoffmann, a bead-like and a nodular phlebitis may appear in secondary syphilis. The first consists chiefly of thickening of the media and intima, the latter of periphlebitis, usually with thrombus formation characterized by numerous giant cells similar to the cells of Langhans. The syphilitic nodose and multiform erythema appearing in the secondary and tertiary stages probably also has its origin in subcutaneous veins (Markus, Hoffman). In syphilitic leucoderma, (see under skin), according to Geber, the cells of the epidermis lose their pigment-producing power on account of chronic phlebitis and gummatous periphlebitis in the skin. See Friboes (lit.) for primary syphilitic phlebitis of small veins in secondary and tertiary lues. In a 19 year old student, about 9 months after infection, Verse saw severe cerebrospinal syphilitic phlebitis with normal arteries (demonstration of spirochaetae),—(lit. in reference to venous syphilis, by Ziegler, v. Eulenburg—3rd, edition, also Thorel, E. IX, 1904, a. XI, 1907; Herzheimer syphilis of veins E. 1907, and Blumenfeld, Derm. Centralbl. VIIth year; Thibierge a. Havaut, finding of spirochetae; phlebitis migrans by Schwarz). Syphilis of vessels, by Benda, in Text Book of Sexual Diseases, Vienna, 1912; cerebrospinal syphilitic phlebitis by Verse, Path. G. 16, 1913, a. Z. B. 56, 1913, lit.

Actinomycosis of the veins is secondary within actinomycotic foci, *e.g.*, in the liver, etc.

### Dilatation of Veins

There are cylindrical, spindle-shaped, serpentine and circoid diffuse dilatations or phlebectasias and saccular, barrel-shaped or nodular partial dilatations, or varices. The different forms merge one into the other. Varicose nodules may be of the size of peas to hen's eggs. From mere distension, the dilated vessels soon show changes in the walls, mostly due to connective tissue proliferation. The formation of a saccular varix is always preceded by an especial local relaxation of the wall. The secondary chronic phlebitis combined with connective tissue production causes gradual

destruction of the elastico-muscular elements and substitution by connective tissue. Inflammation of the tissue adjacent to veins may also be communicated, causing a tendency to ectasia.

B. Fischer saw in the walls of ectatic veins both marked proliferation of cellular connective tissue and massive destruction of elastic fibres; with Cornil and Jores, he believes such inflammatory changes in chronic phlebitis are the actual primary factors in ectasia. But Ziegler is of the opinion that it is a secondary process in an already dilated vein. We ourselves also believe that cause and effect are misplaced in the former theory, and that a greater mechanical functional demand on the venous wall, as from stasis, is the direct cause of connective tissue proliferation, (see Fuchs); indeed, connective tissue proliferation rather causes thickening and even narrowing, than dilatation of the lumen. Marullaz thinks the process begins with hypertrophy of the inner layer which continues to the media and is followed by atrophy, especially of the musculature. Janni describes endophlebitic nodules and plates with destruction of the elastic boundary layer as the beginning of varices. But Scagliosi believes degeneration of the muscle fibres of the media, caused by some inflammation, is the primary factor. Kallenberger (lit.) would have us believe that circumscribed ruptures of the elastica of the intima, interna and externa are important, but he also adds, very carefully, that investigation of isolated cases with variable findings gives no grounds for generalized theory. Zancan (lit.) saw no traces of inflammatory changes, but found atrophy of muscle fibres, fragmentation and degeneration of the elastic elements and connective tissue proliferation, with consequent loss of sharpness between the layers. Thoma, adhering to his theory of arteriosclerosis, (see p. 113), sees the first stage as a phlebomalacia followed by phlebosclerosis.

The structure of the walls of dilated veins varies greatly. Frequently they are thinned at the beginning, become overstretched and remain permanently so. But in other cases, active connective tissue proliferation (phlebosclerosis) begins in the whole wall; it leads to atrophy of the muscular and elastic elements and then to thickening and hardening. In diffuse phlebectasias this process is the more frequent. The proliferation may eventually cause irregularity and noticeable narrowing of the lumen. The vasa vasorum are markedly developed, and often distended.

In older venous dilatations, the perivascular connective tissue also participates in the productive process, so that the outside of the vein shows no distinct boundary. Frequently, thin and thick areas alternate, and the intima is greatly thickened, sometimes hyalin, and bulges into the lumen.

In older phlebectasias, calcification is not rare, sometimes very extensive, in the wall as well as in thrombi. Pigmentation of the wall and its vicinity is frequent, and due to small hemorrhages.

If many bulgings and sacs lie close together they may inter-communicate on account of pressure atrophy of the walls and there results a cavernous system of blood spaces (anastomotic varix). Rounded thrombi are common in saccular phlebectasias, and by calcification become phleboliths (see p. 155).

Rupture of varices causes hemorrhage, which may be fatal, especially when in internal organs, *e.g.*, in the esophagus, stomach, spleen, etc.

Venous dilatations are most frequent in the hemorrhoidal plexus (hemorrhoids), in the legs (varicose veins), in the venous plexus (pampiniform) of the spermatic cord (varicocele), especially on the left side, in the pudental plexus, surrounding the prostate, and the utero-vaginal and vesical plexuses. The left spermatic vein springs from the pampiniform plexus, and enters the left renal vein, while the right empties directly into the inferior vena cava.

Venous dilatation on the edges and base of the tongue, also in the skin of the nose, cheeks, etc., is frequent in advanced age.

In other places, venous dilatations are less frequent, as in the bladder mucosa, the esophagus, (see under cirrhosis of liver), in the pharynx, mesenteric veins, in the bowel walls, (see there), and veins of the pia and brain. The author found ruptured varices of the brain as cause of death in two cases of eclampsia which were just delivered, (see also Anders).

In another case, it was found that a woman after child-birth died of hemorrhage due to uterine atony; the veins of the whole uterine wall showed ectasias almost as thick as a finger, partly diffuse, partly saccular. The uterine atony was easily understood from the findings. Halbau also reported a similar case of phlebectasia of the gravid uterus.

Hedinger described a rare pulmonary varix, and Reinhardt (lit.) phlebectasias and varices of the ischiatic nerve. In reference to true diffuse phlebectasis of arm or leg, a progressive venous dilatation confined to existing vessels and differential diagnosis from extensive cavernoma and venous branching angioma, see p. 150. Comp. Sonntag, Bircher, Bockenheimer. Varices of the auricular septum on p. 155.

In reference to the cause of phlebectasia, the first consideration touches diminished resistance of the wall. This may be a congenital, possibly inherited, weakness (see de Vecchi), or faulty structure of the wall (Kramer).

There are great normal variations in the thickness of the wall of similar veins in different individuals; there are also congenitally stronger and weaker places, the latter of which, according to Bachmann, are probably of importance as starting points of varices. Kocher believes these predisposing structual conditions are "prevaricose," differing only in degree from fully formed varices. Hesse and Schaak find a favorable factor in

the absence of leaflets above the entrance of the saphenous vein, which they demonstrated in 23% of cases, (see Kramer also). Congenital varices by Hasebroek, lit.

In other cases, inflammatory or toxic causes including bacterial toxins in infections (see Zesas), perhaps auto-intoxications, such as those during pregnancy, endanger the integrity of the walls of veins as well as arteries. Then too (*b*) mechanical circulatory obstructions are notorious in their influence when there is maladjustment between in- and outflow, thus

FIG. 92.—Superficial varices of the lower thigh; the skin viewed from the inside; the veins are empty; 4/5 nat. size.

increasing the venous pressure because the backflow impedes the passage of venous blood, *i.e.*, causes congestion.

The difficulty may be due to general causes such as cardiac weakness, cardiac lesions, circulatory interference by pulmonary conditions, action of gravity, or it may be dependent on local conditions, *e.g.*, interference with the portal circulation in hepatic disease. Pressure of a tumor, a truss, overfilled rectum, gravid uterus, etc., have been, or will be, further discussed.

The action of congestion, *i.e.*, of hydrostatic pressure, as a dilating factor is plainly seen in the varices of the lower extremities (varicose veins).

It is known that much standing, an habitual upright posture without sufficient activity of the legs, especially in long legged individuals, predisposes to varicose veins. The explanation of this is that the suction mechanism in the vicinity of the foramen ovale is inoperative if leg action is suspended, but during motion, the alternating tension and relaxation of the confluent venous inflow forms a sort of suction heart (Braune). Of less importance is the absence of muscle activity with its intermittent compression of the venous walls. If once the veins are dilated by congestion, a slight relative insufficiency of the valves develops very readily, for since they retain their former length, while the vessel wall stretches, they become too short and thus permit backflow of the blood (Magnus). With the body in the upright position, the blood in varicose veins may actually flow from above downward; in the horizontal position, the current flows toward the heart. A vein dilated for a long period never recovers its normal caliber.

An important role in the formation of saccular varices is played by the valve rings which appear simultaneously with the varix, and which are actually firm annular areas at the insertion of the valves. They may be quite easily seen on the trunk of the saphenous vein when cylindrically dilated. If the venous wall as a whole gives way to the hydrostatic pressure because it is congenitally too weak, or because the vessel is constantly overloaded, the firmer valve rings participate but very slightly.

If hydrostatic pressure alone sufficed to form these varices, then their greatest diameter would lie above the stationary, narrow, valve ring (proximal). But as Ledderhose demonstrated, the contrary is the case, because the blood stream, forcing its way and causing congestion in front of the ring distally—as "vis a tergo," bulges the wall only in front of the valves by the lateral pressure; in this way is produced the typical varix, the diameter of which is largest below the valve (distal), and not, as might be expected, above the valve (proximal). It is like a bottle with its bottom turned up. (Other theories by Hasebrook, Magnus.) Leg varices involve chiefly the subcutaneous ramifications of the large saphenous vein, uni- or bilateral. Usually it is first noticed under the thin skin on the median side of the tibia. Later, massive worm-like or knotted convolutions develop. The term "krampfadern" is justified, because abnormal muscle spasms frequently occur owing to deep seated varices. If, as in the Trendelenburg operation for varicose veins, the saphenous vein is ligated at its upper end, back flow and back pressure of the blood from the femoral vein into the saphenous are prevented; the blood can flow off from the leg through the deeper vessels, especially during walking. The success of this operation in many cases emphasizes the importance of hydrostatic

pressure. But in other cases, the result is reached only by numerous ligations of anastomoses (see Kocher, etc., Hasebrock).

In hemorrhoids, (the most frequent form of phlebectasia), the mechanical factor of constant constipation is added to by inflammatory conditions such as catarrhal changes in the mucosa, caused by fecal retention, which continue to the venous walls and predispose them to dilatation. But, on the other hand, the anatomical peculiarities of these veins must also be considered. The hemorrhoidal ring of venous loops and ampullary venous distensions is normally and frequently seen in children; there is also the hemorrhoidal venous plexus. These peculiar conditions, not well understood, led to the opinion of Reinbach-Harttung, that hemorrhoids are always angiomas, a statement which was denied in toto by v. Ruediger-Rydygier, Torikata (lit.), Silverberg, etc. Venous stasis alone is able to provoke relatively slight varices. Fecal retention is the frequent factor in overloading the plexus, as well as the veins of the hemorrhoidal region as a whole. According to Schmincke, (a. Szuman, lit.), pressure of the fecal column during defecation forces blood into the small venous ramifications, while the abdominal pressure prevents quick outflow. Later, inflammatory changes are added, and atrophy of elastic fibres and muscular elements causes further dilatation. The dilated veins may appear as nodules in front of the anus. They bleed readily, especially during defecation, (see under rectum). The hemorrhoidal vessels have a double outflow, one to the portal vein, and one through the pelvic plexus to the cava. It is difficult to explain these ectasias by simple stasis, without considering all of these anatomical peculiarities. On the other hand, the outflow conditions are favorable to the embolic transportation of thrombi, for instance, in operations for hemorrhoids.

A marked collateral distention and contortion of veins of the anterior abdominal wall which converge radially to the umbilicus is called the "caput Medusae," and develops if passage of blood through the portal vein to the liver becomes more or less impossible by reason of thrombosis, cirrhosis of the liver, etc. The following vessels compensate: the hypogastric, spermatic, veins of the renal capsule, of the esophagus (these may be dilated to varicosities causing fatal hemorrhages), the inferior epigastric, internal mammary, and intercostals, which lead indirectly by way of the azygos and hemiazygos, and directly into the superior cava. Sometimes branches of the portal as thick as a lead pencil enter the suspensory and teres ligaments through the reopened, or persistent umbilical vein, or its channel to the anterior abdominal wall (Baumgarten). See Thomas and Saxer (lit.), and Gilbert and Villaret for details of these complicated conditions. In obstruction of the inferior vena cava by simple, or tumor thrombi, there occasionally develop massive, worm-like

dilatations and varices to the thickness of a finger on the anterior abdominal wall, reaching up to the axilla, and under the mammae. The anastomoses between the epigastric and the internal mammary vein supply the collateral circulation (lit. by Globig). If the superior cava is occluded (rare), wide collateral cutaneous veins develop, especially on the anterior thoracic wall up to the neck, particularly if the azygos vein, by which drainage of the upper half of the body might be accomplished, is also occluded. The mammary and the epigastric are also helpful vessels.

FIGS. 93–94.—Ring of thick inner hemorrhoidal nodules, a thumb's breadth above the anal ring; man 59 years old with pulmonary emphysema and cardiac hypertrophy, died of broncho-pneumonia. Cross section of nodules shows their honeycombed structure; both ⅞ nat. size.

The consequences of phlebectasias to the tissues in which they are located are venous congestion, edema (blood serum passing outward into the tissues), increased secretion of sweat by the skin, persistent catarrh of mucous surfaces, and frequent hemorrhages. The skin, especially over the varices, frequently shows thinning, epidermal desquamation, and eczema (varicose eczema). The chronic congestive edema of the skin is followed by fibrous induration and thickening of both the skin and subcutaneous tissues.

This is frequently augmented by oft recurring inflammations to which the easily vulnerable tissue is constantly exposed, and by lymphangitis.

In this way, a shapeless thickening develops (phlebectatic elephantiasis), most frequently occurring on the legs below the knees in which the epidermis may proliferate in the form of warty excrescences. The bones, with or without ulceration, possibly show an active ossifying periostitis (see illustrations under bones and skin).

The opinion held by Zinsser and Philipp that changes in the bone of the lower leg in leg ulcer are of syphilitic origin in the majority of cases cannot be entertained (see also Kottmaier, Scherber, Nobl, Morris).

Torpid, deep, sometimes circular tumors or varicose tumors (fig. 95), with calloused bases and margins, frequently follow slight inflammations or mechanical injury. Thickened bone may frequently be seen in the base of the ulcer. To this may be added that there is a tendency to erysipelas, skin abcesses and inflammation of the sebaceous glands (furuncles).

The hard, infiltrated, fragile veins tear during the slightest trauma (rupture of a varix) and cause massive, sometimes fatal, hemorrhages. Embolic thrombi carried into the pulmonary artery may cause sudden death, as the author has repeatedly seen; thrombophlebitis and lymphangitis are some other dangerous complications.

Carcinoma sometimes develops in the base of a leg ulcer (see fig. 96, and under skin). The tibia and fibula may be infiltrated, become carious and hollowed out with subsequent fracture. The author observed a case of this type in a woman 86 years old who had had a leg ulcer for 50 years. As another result of the varicose symptom complex, onychogryphosis (see under skin) is sometimes seen.

### The Relations of Tumors to Veins

Tumors quite frequently rupture into veins, occlude them more or less completely (tumor-thrombi), grow into the vessel lumen, or are detached and carried as emboli to distant parts. This is most frequent in sarcoma and carcinoma, often in malignant tumors of the thyroid, and especially in hypernephromata and the malignant chorioepitheliomata.

Lymphogranulomas, like malignant tumors, also infiltrate the walls of veins (lit. by K. Mayer).

Small veins may be much dilated by tumor masses. The author, for instance, saw a sarcomatous uterine myoma in a 60 year old woman in whom the right ovarian vein was filled to the thickness of a thumb with glassy, grayish red, soft tumor masses.

In sarcomas the tumor cells are prone to rupture into capillaries belonging to the tumor itself since they have a tendency to bleed, because their endothelium may be directly in touch with tumor cells. For this reason, the dissemination of tumor cells in sarcomas occurs chiefly by

way of the bood, (exceptions, see under lymph vessels). In sarcomas, the cells are embedded in the intercellular substance and adhere more firmly than in carcinomas, hence emboli larger than in carcinomas are frequently observed.

Malignant chorioepithelioma is similar to sarcoma in this respect, as well as in respect to the dilatation of capillaries and hemorrhages; the metastases are usually via the blood,(see fig. under lung and brain).

In a sarcoma arising in the bone marrow of the femur, for instance, we find the marrow veins, branches of the profunda femoris, filled with sarcomatous masses. If particles are detached, they are carried into the femoral vein, cava, right heart, lungs (tumor embolism), where they develop into metastases. After invasion of the pulmonary veins further metastases are spread. Sometimes the cardiac valves intercept such embolic tumor masses (see p. 85, fig. 35).

Invasion of carcinoma into veins occurs more frequently than was formerly supposed. According to Goldmann, in the very beginning of carcinoma, a proliferation into the veins is likely to occur—a statement which can easily be verified, especially in gastric and intestinal carcinoma with metastases to the liver (portal). In this way, carcinoma of the intima is produced (comp. Thaysen). Fortunately this does not usually affect the general character of the spread of carcinoma which favors lymphatics, because in many cases the cells which get into the blood and so into the lungs (see lungs), perish. But in secondary carcinoma of the liver, as after primary carcinoma of the stomach, coarse rupture into the hepatic veins is often seen. Sometimes tumor emboli can be demonstrated macroscopically in the branches of the pulmonary artery; microscopically they are quite frequent (see under lung).

In metastatic carcinoma of the lung, macroscopic invasion into the veins is often found (Weigert-Pollak). This is also true of sarcomas. In a man 63 years old, with carcinoma of the gall bladder and cholelithiasis, the carcinoma masses had passed the thoracic duct and grown massively into the innominate and left subclavian veins, and thus reached the lungs partly as emboli; tumor and hemorrhagic infarction were plainly seen.

In studies of gastric carcinoma by Foersterling and Schlagenhaufer, even the peripheral veins showed carcinomatous infiltration, induced by way of the lymphatics; they cause both parietal, and occluding thrombi; some of the latter became recanalized. This produces the clinical picture of so-called migrating thrombophlebitis.

Rupture of a chondroma into a vein with the formation of metastases also occurs, although rarely, as in the celebrated case of C. O. Weber. It is important in relation to the classification of chondromas and in the

teaching of tumor emboli. In a 25 year old man with numerous symmetrical exostoses and enchondromas of the whole skeleton, rupture of a large, soft, pelvic enchondroma occurred into the pelvic veins and was followed by numerous metastases in the lungs and liver. The author has seen both cases of this kind, and cases like that of Ernst, in which there was a vertebral enchondroma which ruptured in many places into veins but, in spite

FIG. 95.—Large circular crural ulcer, base and margins calloused. In the base the thickened tibia, on surface carious, hard edema of the leg (clinically mistaken for carcinoma).

FIG. 96.—Circular carcinoma (cornified) in a 50 year old crural ulcer. Spontaneous fracture of tibia and fibula infiltrated by carcinoma. Woman 86 years old.

of the presence of emboli in the pulmonary arteries, no metastatic nodules were found in the lungs. Furthermore, rupture into veins and metastases are seen frequently in myxomas, and are relatively frequent in certain malignant tumors of the kidney (see kidney).

It must also be remembered that tumor transportation may occur in a vein against the current; tumor fragments are carried backward by a receding wave (retrograde metastasis, Heller; retrograde transportation v. Recklinghausen). The venous negative pressure becomes positive for

the moment if intrathoracic pressure is suddenly increased, as in emphysema, tricuspid insufficiency, or aggressive coughing, or compression of the thorax. A wave is thus sent backward (lit. by Thorel and Risel, Yatsushiro, Ribbert—compare similar conditions in infectious embolism in which liver abscesses follow an infectious sinus thrombosis; see under liver abscess).

Not infrequently, tumor masses occlude a vein and grow in the retrograde direction (retrograde tumor thrombi; comp. observations of the author under spleen).

Phlebectasias and capillary ectasias are often found in vascular tumors.

Primary tumors of the venous wall are quite rare; leiomyomas have been described, some with peg-like intravascular extensions (Aufrecht, Bottchr, Cernezzi, Ecoffey, lit., Sitzenfrey, Schnyder, lit.); an endothelioma described by Unruh; an endothelial sarcoma (Oberndorfer), an enchondroma (Picchi), sarcomas (Sick, Brohl), a myosarcoma (Perl), a similar "phlebosarcoma racemosum" (van Ree), an angiosarcoma springing from varices (Borchard); phlebogenous angiomas on page 172.

### Parasites

Occasionally, echinococci in the liver rupture into an hepatic vein and cysts are carried into the right heart and lungs,—for details, see under liver. In reference to distomum, see parasites, under intestines.

The invasion of vegetable parasites is of great importance, especially pyogenic organisms. Bacteria carried by the veins (infected emboli) cause metastatic abscesses.

### Capillaries

**Reaction of Capillaries in Inflammation.**—In exudative inflammation, *e.g.*, pneumonia, the capillaries become dilated and permeable to fluid and cellular blood constituents.

The latter pass through so-called stomata (p. 97). Leucocytes migrate actively. The motionless, but very elastic erythrocytes escape passively by diapedesis or by rhexis. The escape of purely fluid elements depends on transudation as discussed on p. 2. A similar process is observed in small veins.

In productive inflammation, the endothelial layer becomes thickened, protoplasmic buds become patent, and thus form new vessels.

**Degenerations.**—The most important change is fatty degeneration (fig. F, p. 99). Fat granules are deposited around the endothelial nuclei; later, the cells are filled with fat droplets.

This change is common in a variety of inflammatory or degenerative processes in the brain, kidneys, uterus, breasts, etc., especially in blood

dyscrasias such as anemia, intoxications, poisonings from phosphorus, carbon monoxide, toad stools, infections, tumors, particularly if malignant. Rupture and capillary hemorrhages are frequently the result.

For hyalin and amyloid degeneration, see under arteries (pp. 106 and 107).

Calcification of the capillaries of the brain is frequent in advanced age. Hyalinization often precedes the change, *e.g.*, in the thyroid gland. Calcified capillaries are also found in "calcium metastases."

**Dilatation—Narrowing—Occlusion.**—Dilatation is seen most frequently in pulmonary congestion, in tumors such as carcinoma and sarcoma, etc. In hemangiomas, tumors consisting of newly formed capillaries, dilatation of capillaries and of veins and arteries is frequent, (hemangioma cavernosum).

Narrowing and occlusion may be due to inflammation, compression, thrombosis, embolism, etc., (see below).

Thrombosis may be brought about by coagulation of erythrocytes, leucocytes, fibrin and blood platelets, or by fusion of colorless red cells, or by clumped platelets or fibrin (coming from blood plasma). They are known as hyalin capillary thrombi. The influences at work are toxic, infectious, etc.

**Hemorrhages.**—Capillary hemorrhages occur by diapedesis or by rhexis. The first is seen best in pulmonary congestion; the latter is assumed to occur in various poisonings such as phosphorus, arsenic, etc., in infections, and in the blood dyscrasias such as congenital hemophilia, or the acquired hemorrhagic diatheses. Changes in the wall and the endothelium and general circulatory disturbances may all share in causing rupture. Frequently the serous membranes, in other cases the skin, are the seat of numerous capillary hemorrhages.

Blood platelets are active in stopping a hemorrhage due to rhexis by causing capillary occlusion.

**Emboli.**—They are frequent in the capillaries and are chiefly due to fat, (see under lung); bacteria (see p. 41), parenchymatous cells (see embolism of lung), air, and tumor cells (see under lung).

**Tumors.**—Capillary hemangiomas are composed of newly formed capillaries.

If they are markedly dilated they are called cavernous angiomas, and often resemble simple capillary ectasias, (more details and illustr. under skin).

Plexiform angiomas (telangiectasias) often show a tendency to spread and are found in the skin of younger children, being congenital in origin, (blood marks, birth marks, vascular naevi). Vessel proliferation usually remains, but the formation of hyperplastic vessels and dilatation stops, (see illustr. under skin).

Angiomas may also develop from arteries and veins. If they arise in the venous wall from the vasa vasorum, they are the so-called phlebogenous angiomas (Virchow, v. Esmarch, v. Recklinghausen, L. Pick), in which, according to Virchow, blood its carried by its own arteries into the blood spaces.

See under endothelioma p. 178, and under "sarcomas of the dura mater, the thyroid, uterus and skin" in reference to sarcomatous tumors springing directly from blood vessels.

## LYMPH VESSELS

**Anatomy.**—Lymph capillaries consist of tubes of single endothelial cells. The larger vessels have a wall proper resembling that of a vein, but with important differences. Below the endothelium is a peculiar interweaving network of bundles of muscle fibres which are arranged more circularly in the outer layers and in which elastic fibres may be differentiated. In medium-sized lymph vessels, they are not arranged circularly as in veins, but as fine strands spun around the muscle fibres as in smaller arteries; this fibre network is not sharply differentiated from its surroundings. Lymph capillaries have no valves, but actual lymph vessels are abundantly supplied. The larger trunks, especially the thoracic duct, show thicker elastic fibres in their musculature permitting the differentiation of an inner and an outer limiting membrane, and in this respect they resemble an artery.

It is not true, as was formerly supposed, that peripherally, the lymph capillaries are open, and communicate with the lymph spaces of the connective tissue. It has been shown in lymph capillaries and in cul de sacs, that tissue lymph does not enter the capillaries through preformed channels, but by osmosis (McCallum). Occasionally, dilated, but not preformed, intercellular spaces (stomata) also permit the passage of cellular elements. See anatomy of the lymphatic system by Bartels, lit., Schaffer, and others.

The thoracic duct collects all of the lymph and conducts it into the venous system. It is formed by the two lumbar lymphatic trunks which collect from the lower extremities, the genitalia, the pelvis and the abdominal wall, and by the intestinal lymphatic trunk which collects the chyle lymphatics (intestinal lymph), and empties, according to Eossifow, chiefly (up to 70%) into the left lumbar trunk. The collecting place of the trunks shows a dilatation, the chyle cistern, the position of which varies. The low position is at the level of the second lumbar vertebra, the high position at the eleventh or twelfth thoracic vertebra. The duct passes through the diaphragm, through the aortic foramen, and continues posterior in the connective tissue of the mediastinum between the aorta and the

azygos vein, *i.e.*, to the right of the midline. It then turns somewhat to the left in front of the fourth thoracic vertebra, crosses the arch of the aorta and rises on the longus colli muscle to the sixth cervical vertebra to empty into the left subclavian vein shortly before its junction with the left common jugular vein, after the roots from the upper trunk of the left jugular and left subclavian have been incorporated.

To find it quickly during dissection, it is best to follow Koster's method. After removal of the heart and the left lung, the right lung is lifted up and without separating it at the hilum, is placed into the empty left pleural cavity. The region of the thoracic part of the duct with the azygos vein thus becomes firmly stretched and separated while the esophagus is displaced to the left. After opening the thin pleura, it is easy to free a large section of the duct in situ. It is advisable for beginners to tie a thread around the exposed section and proceed with further exposure only after the cervical organs, aorta, and all of the mesentery have been removed.

### Inflammation of the Lymph Vessels. Lymphangitis

**Acute Lymphangitis.**—Several lymph vessels are always involved with the adjacent tissue in which they are embedded—peri and paralymphangitis—indeed the latter involvement is often the chief symptom since a phlegmonous inflammation spreads in the direction of the lymph stream.

Injurious agents enter the wall of the lymphatics from without, as in absorption from an inflamed area, and the vessels themselves, injured during the process, carry the injurious substances, perhaps for long distances.

Lymphangitis is divided into simple and purulent.

In simple lymphangitis, the tissue in the vicinity of the vessel appears injected, edematous and infiltrated. Sometimes ecchymoses make their appearance from the hyperemic adventitia. The wall of the lymph vessel is saturated with inflammatory exudate, and is thickened; its endothelium swells, and may look like epithelium, as it multiplies or desquamates.

The lymph remains fluid or coagulates in the smaller vessels. Simple lymphangitis heals quickly after absorption of the exudate and endothelial regeneration, or becomes chronic, or progresses to the purulent form.

Proliferating exudative endolymphangitis occurs, *e.g.*, with perilymphangitis, in gonorrhea (Nobl).

In purulent lymphangitis, streptococci are probably the most common causative organisms.

When bacteria, toxins, or pus enter the walls of a lymph vessel, they become stiff and thickened, pus collects in the adventitia and neighboring tissue (phlegmonous inflammation), the contents of the vessels are altered, and the endothelium swells, desquamates and disintegrates. This is

spoken of as "thrombolymphangitis," analogous to "thrombophlebitis" (see there). Lymph vessels distended to the thickness of a lead-pencil with pus or puriform masses are yellow and suggest a chain of beads, (see, *e.g.*, in acute interstitial pneumonia, influenza). Constrictions between the beaded swellings correspond to the firmer attachments of the valves, (see in purulent parametritis, especially puerperal). The walls suppurate and open into abscess cavities in the vicinity; isolated abscesses in the neighborhood are quite frequent. Extensive phlegmons and joint or lymph node suppurations are not unusual accompaniments. Infectious lymph, when carried further, enters the blood and initiates a general septico-pyemia.

The clinical picture of simple acute lymphangitis of superficial vessels is seen most frequently in small infected injuries of the hands (infection during autopsies), or of the feet (infection after removal of corns), and is very characteristic. Red striae, hyperemia of the adventitia, painful to pressure, extend to the elbows and axillary nodes. A phlebitis or phlebitic thrombosis may be combined (p. 157).

**Chronic Lymphangitis.**—Chronic inflammations appear in larger vessels as proliferation and indurations of the walls and vicinity which occlude the tube in time, (fibrous obliterating lymphangitis). The result is lymph stasis. Endothelial proliferation predominates in the smaller vessels; as the cells enlarge and become like epithelium, the vessels appear like obstructed glandular or carcinomatous columns and tubes, (productive lymphangitis, proliferating endolymphangitis; illust. 1).

Both forms are often seen in chronically inflamed serous membranes, especially over the lungs, and within these organs. But as illustration, 1, p. 180 shows, there may be pronounced productive endolymphangitis within metastatic tumor nodules of the lung. The interference with absorption is often of serious moment on account of later exudative processes in the lung, as emphasized by Koster.

In anthracosis of the lungs (see there), atrophy of lymph vessels plays a part in determining the picture.

Chronic lymphangitis and perilymphangitis of extraordinary proportion develop in glanders of horses and cattle. The lungs show greatly enlarged lymph vessels surrounded by fibrous tissue.

**Specific Inflammations.**—Tuberculosis of lymph vessels. Lymph vessels play an important role in the dissemination of tuberculosis, not merely within the lung, but in the whole organism. The relations are seen most frequently and clearly in the chyle vessels of the intestinal serosa and sometimes in the mesentery in the vicinity of a deeply situated tuberculous abscess of the intestinal mucosa.

Whitish gray nodules appear on the serosa under an ulcer which perhaps shines through and is dark red in appearance. The nodules are

ordinarily in vermiform strands like beads, partly on the serosa, and partly in the mesentery as far as a lymph node. The strings may be varicose due to lymph stasis. The formation of the nodules depends partly on tuberculous lymphangitis, and partly on tubercle formation with caseous degeneration within the lymph vessels starting from the endothelium, and therefore actual tuberculous lymphangitis.

Tuberculosis of superficial lymph vessels is occasionally peripheral to tuberculous ulcerations, *e.g.*, in lupus of the hand. Nodules, beads and abscesses develop along the course of the lymph vessels. A leg thickened from elephantiasis may show these along the saphenous vein (Jordan).

Tuberculous changes appear in the thoracic duct, as Ponfick first showed in miliary tuberculosis. They are seen as submiliary to large conglomerate tubercles and cheesy ulcers, the latter often on the valves. Sometimes only a small area is affected, most frequently the upper end. In other cases, the entire intima is covered, or the entire duct becomes caseous, or shows varicose dilatations containing caseous or whey-like masses. The author found a stiff system of cavities about the cisterna, some the size of peas, some caseous and others spotted by hemorrhages. It has been found in children, and in quite old phthisics. Infection of the duct, as a rule, arises from caseous lymph nodules (retroperitoneal, mesenteric, mediastinal), and when the caseous material is in contact with the lumen of the thoracic duct, the passing lymph current may receive sufficient tubercle bacilli to cause acute general miliary tuberculosis, as demonstrated first by Weigert.

Retrograde lymphatic infection is also common. In endothoracic tuberculosis, diseased para-aortic lymph nodes are occasionally the only abdominal tuberculous foci, (see Tendeloo, and under pulmonary tuberculosis).

Other specific inflammations of the lymph vessels (syphilis, glanders, leprosy) are rare. For inflammation of lymph vessels in the initial sclerosis, see under syphilis of skin.

### Closure and Dilatation of Lymph Vessels

**Lymphangiectasis.**—Ectasia is occasionally peripheral to obliterating lymphangitis if the collaterals do not suffice, as after occlusion by simple obliterating lymphangitis, carcinoma, tuberculosis, or contraction of surrounding tissue or tumors.

It occasionally extends to lymph nodes which become a finely reticulated, honeycomb-like network (lymph adeno-cystoma, adenolymphocele) as the sinuses enlarge (see Orth, Odenius, Gregarsen). The author saw this in mesenteric nodes following extensive occlusion of lymph channels by a round cell solid carcinoma starting from the prostate.

It develops chiefly in small branches; thus, in tuberculosis, the lymphangitis involves the mesenteric chyle vessels. Muscle hypertrophy in the dilated vessels may occur. Materna saw vesicle-like ectasias of lymph vessels of the pulmonary pleura in status lymphaticus due to greater filling and impediment to the outflow by cardio-valvular lesions.

FIG. 97. -Elephantiasis of right arm existing for 1½ years; from a woman 58 years old with slow growing carcinoma of right breast. The chronic edematous parts have shrunk in wrinkles in the alcohol; 2/9 nat. size.

The thoracic duct undergoes ectasias at isolated areas, or throughout its length. If the constricting factor, usually a tumor, is at the upper end, the duct is sometimes dilated to the thickness of a thumb, while the cysterna may be larger than a hen's egg (rare), or appear like a cyst as large as a fist in Enzmann's case, (see also Carbone, Sankkuhl). Sometimes no ectasia develops even if the main trunk is occluded, for collaterals carry the lymph around the obstruction.

Stasis may continue into the smaller vessels; yellow dots, varicose striae and thicker strands appear in the intestinal mucosa or in lymph vessels of the mesentery while plaques of exuded lymph add to the characteristic picture.

Lymphorrhagia is due to bursting of the overfilled thoracic duct, or more frequently, one of its branches. It is followed by chylothorax or chylous ascites, (both very rare). Usually the chyle pours into an exudate already present.

In the skin, edematous saturation and connective tissue hyperplasia are added to the chronic lymphangitis, productive perilymphangitis and ectasia of the lymph vessels which occur from complete removal or atrophy of the regional nodes. The combination causes lymphangiectatic pachydermia, as in leg ulcers, after removal or destruction of the inguinal nodes in bubo, etc.; or in the arm after operative removal of the axillary nodes or their isolation in mammary carcinoma; or perhaps involving only the vulva (lymphatic hyperplasia), in atrophy of the inguinal nodes. A higher degree of hyperplasia showing tumor-like solidity is called elephantiasis. Lymphangiectatic elephantiasis

is distinguished by its wide and varicose lymph vessels (comp. under blood and see fig. 97 and under skin).

### Tumors of Lymph Vessels

**Lymphangiomas.**—These are variously shaped, diffuse, or circumscribed neoplasms, the chief constituents of which are spaces lined with endothelium and containing lymph. The spaces in some cases are enormously distended; in others, the walls are remarkably thickened.

It is often difficult to say in an individual case whether a mass is a true neoplasm of lymph vessels, or only dilatation with secondary thickening of preformed vessels and some muscular hypertrophy. According to M. B. Schmidt, lymph stasis is important, inasmuch as it leads to muscular labor hypertrophy of the trunks. The fibres when hypertrophic are arranged in interwoven bundles which also appear in the connective tissue between the enlarged lymph spaces.

Fig. 98.—Congenital cystic hygroma of neck (cystic lymphangioma), unusual on account of bilateral symmetrical development; male infant, died 10 hrs. after birth; ⅓ nat. size.

But a lymphangioma is essentially a neoplasm; retention phenomena may be added secondarily. Sick believes the starting point of many lymphangiomas is an isolated vessel or connective tissue primitive rest which proliferates into new lymph vessels.

Wegner's classification of lymphangiomas is convenient in differentiating the various forms.

(*a*) A simple lymphangioma is a circumscribed tumor consisting of net-like connected capillary and larger lymph vessels, (situation, skin, tongue, etc., see illustrations).

(*b*) A cavernous lymphangioma shows larger lymph spaces lined with endothelium and surrounded by more or less firm fibromuscular dividing walls. It is found as macroglossia (lymphangiomatous form in contradistinction to the hemangiomatous form), macrocheilia, more rarely in other parts of the face and skin,(see under mouth and skin). Macroglossia may be congenital, and as such impedes breathing and swallowing.

(*a*) and (*b*) tend to grow in those parts of the body which show clefts during fetal times (fissure lymphangiomas).

(*c*) Cystic lymphangiomas, also called congenital cystoids, or congenital cystic hygromas, consist of cysts, simple or subdivided, lined with endothelium; the contents are clear, serous, milky, or chocolate colored fluids

containing cholesterin and detritus. They appear chiefly in the neck, the arm (axilla), breast, shoulder, lower sacral regions, abdomen, thigh, inguinal region, etc. When in the mesentery, they often contain chyle (chylangioma). In rare cases, large cystic lymphoangiomas have impeded parturition.

The classic congenital cystic hygroma of the neck (Wernher), starts in the submaxillary region, sometimes grows quite rapidly, and may hang downward as a nodular tumor finally reaching the sternum. In other cases, it grows into the face and appears at the base of the buccal cavity. Isolated small cysts may be deep seated between the organs, and even in the vertebral column. The skin covering is smooth or wrinkled or thickened as in elephantiasis. Such patients usually die early, on account of swallowing, respiratory and circulatory disturbances.

Natural recovery by rupture is very rare. Koester demonstrated an endothelial lining in the anastomosing cysts. (See Sick and Henschen, lit., in reference to lymphangiomas.)

**Endotheliomas in General.**—Endotheliomas arise from endothelial proliferation of lymph vessels, lymph spaces of connective tissue, and blood vessels.

As is well known, they also occur in the reticulum of adenoid tissue and in the meningeal lymph spaces. The serous cells of the pericardium, pleura, peritoneum, etc., are often called endothelium (R. Volkmann), but they are mesenchymal cells, and differ from lymph endothelium; they may form fibrillar connective tissue, but no lymphoid cells (comp. Marchand). The conception "endothelium" is the subject of much controversy (His). Some authors call the lining cells of lymph and blood vessels, "epithelial" (Stohr, Fr. Merkel, Schaffer), thus modifying the doctrine of the endotheliomas. But while the conception "endothelium" should not be abandoned, we believe that a sharper definition within neoplasms is advisable, even from a practical viewpoint.

The perithelioma and its derivative tumors, are likewise subjects of controversy. Originally, by the "perithelia," we meant the endothelial cells of perivascular lymph sheaths such as in some organs (brain, testicle, etc.). Later we spoke of perithelia of the adventitia of capillaries of some blood vessels, or, in more general terms, the outermost flat adventitia cells (lit. Bertholet). The so-called perithelia were of special importance in characterizing certain sarcomas described by Eberth, Waldegar and others, first as angiosarcomas, a term, the conception of which, according to our opinion, has its justification even today (see following section). Indeed, there are many authors who would eliminate completely the conception "perithelioma," because a perivascular arrangement may appear in the most diversified tumors, even in those of epithelial origin, and thus there

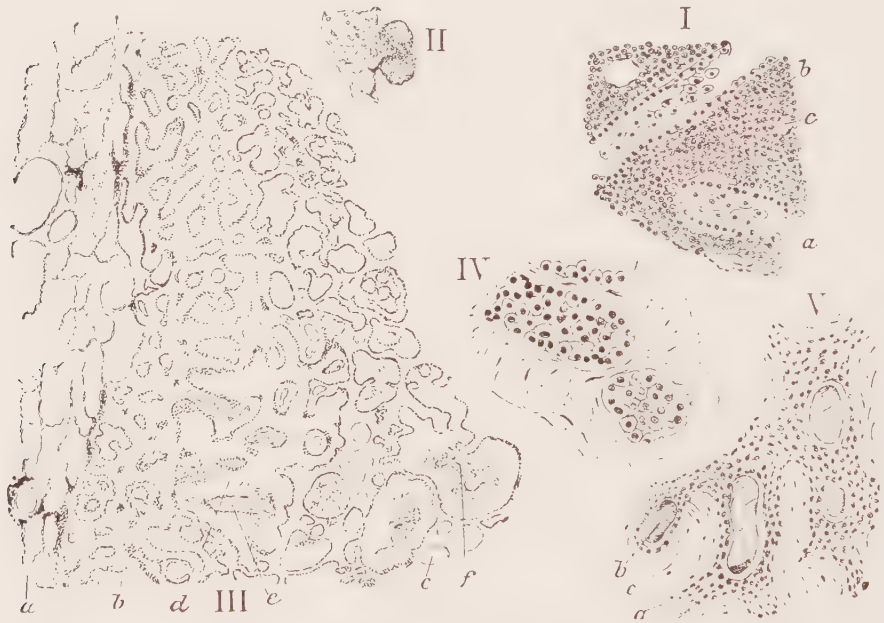
is no safe theoretical starting point for the derivation of the elements of perivascular tissue (see Roussy, Amenille and Nadal). On the other hand, Borst recognizes the possibility of peritheliomas in many organs—in the soft meninges, the choroid plexus, brain, serous membranes, bones, kidneys, muscles, skin, lymph nodes, ovaries, etc.

The rare endotheliomas springing from blood vessels are called intravascular endotheliomas (angiosarcomas or hemangiosarcoma intravascular), or endothelioidal (Bizozzero), or hemangioendothelioma intravasculare (lit. by Hansen). They may occur systemically, *i.e.*, appear simultaneously in various organs (Muller, lit.; v. Hansemann, Schreiber). The unsatisfactory term "endothelial adenoma" is sometimes given to the peritheliomas starting from the perithelium, or, according to v. Rosthorn, "prevascular endothelioma" (lit. by Bevacqua), or, more generally, "perivascular hemangiosarcoma," (comp. under tumors of the bone marrow). Borrmann differentiates hemangioendotheliomas, consisting of vessels with their own walls, which produce only an endothelial proliferation into the lumen, and capillary endotheliomas, which consist of newly formed neoplastic capillaries. But the author has seen sarcomatous hemangioendotheliomas (see illustr. under thyroid), which produced not only new capillaries proving their descent from hemangioblasts, but also endothelial proliferations into the lumen similar to lawlessly growing capillary buds and immature endothelium; there were also independent clumps and columns of polymorphous sarcoma cells elsewhere. See under dura mater for more details in regard to hemangiosarcomas which are demonstrably derived from blood vessel elements of which they possess great numbers. (Borst speaks of atypical neoplasms with angioblastic type of growth.) See under "general observations re sarcomas" for illustrations, also under bones (see R. Meyer). For multiple hemangioendotheliomas in different organs, see Muller, and compare with tumors of the spleen.

Among the endotheliomas, those which spring from the endothelium of lymph vessels with walls proper, and those from the delicate lymph spaces of the connective tissue—lymphangio-endothelioma, lymphangiomatous endothelioma—must be especially mentioned.

(*a*) Tumors from the lymph vessels of the surface of large body cavities, especially pleura and peritoneum, but doubtless in part from lining cells also, may be called endotheliomas (comp. Borst; see under pleura). These rather rare tumors extend to neighboring cavities, may cause true metastases, and were formerly called endothelial carcinomas. This latter name should be dropped, of course, since true carcinomas spring only from epithelium. The tumor consists, microscopically, whether primary or metastatic (comp. Pollmann), partly of cleft-like or gland-like ducts, or

wide irregular spaces, lined with polymorphous, flat or higher cells, (see p. 180, illust. III), and partly of solid plugs, strands and groups of many-shaped large, joined cells (illust. IV). Giant cells, exceptionally rich in chromatin, frequently develop from the proliferating endothelium of lymph vessels and spaces (Glockner). The spaces mimic adenomas, and carcinomas even more so, especially because of papillary formations (illust. III, p. 180). If the tumor progresses in the lymph spaces and lymph vessels, as a rule, their endothelium is hardly recognizable, because,




FIGS. 99–103.—I. Proliferation of endothelium of lymph vessels within a metastatic small round cell sarcoma nodule of lungs; (macrosc, pict. of lung, see under lung!); a, lymph vessels with epithelium-like thickened endothelium; b, round cells of sarcoma; c, capillaries (medium magn.). II. Endothelioma of the pleura, independent nodule with almost general thickening of left pleura, partly diffuse, brawny; partly circumscribed soft nodular (details of this case under pleura) $^{9}/_{10}$ nat. size. III. Endothelioma of the pleura; microscopical low power of illustr. II; a, lung; b, pleura; c, blood vessel; d, hollow space within; e, folds of the wall covered with endothelium cut through with blood vessels of the interstitial tissue cut lengthwise or across; f, endothelial surface. IV. Starting from the same endothelioma of the pleura, solid endothelial plugs (carcinoma-like) proliferating through the diaphragm (medium magn.). V. Cylindromatous lymphangiomatous endothelioma of the parotid (so-called), taken from a hard tumor the size of a walnut which was shelled out of the left parotid of woman 54 years old. Operated; a, formerly considered endothelial, now epithelial cell proliferation; b, hyalin cylinder within; b, gland-like lumen; c, fibromyxomatous interstitial tissue (med. magn.).

it is said, it at once participates in the tumor formation,—so-called regional infection. The transition of flat typical endothelium in lymph vessels into higher atypical form in the same tube, is given as chief supporting evidence for this assumption (see opposed, Ribbert). It is further supposed that the endothelium in touch with the tumor cells simply swells

and can only occasionally be differentiated from the latter (comp. habit of carcinoma, p. 183).

(*b*) Endotheliomas of the delicate meninges of the brain and spinal cord (see there).

(*c*) Endotheliomas of ovaries (see there).

(*d*) Endotheliomas of the dura mater. In some of these, the endothelial cells lie in small strands opposite and flattened against each other, between many connective tissue bundles. The cell clumps and the fibrous bundles are interwoven with each other. Both tissues have their origin in preformed dural elements. If both factors maintain their equilibrium in the growth of the tumor, a fibroendothelioma develops (fibrous or interfascicular endothelioma; see details under psammoma of the dura). If endothelial clumps predominate, it is an alveolar endothelioma, differentiated from carcinoma by the complete attachment of the alveolar contents to its walls. Sometimes, but more rarely, there are thick, branching plugs of laminated, mutually compressed endothelial cells, containing within them a granular mass of debris caused by degeneration (fatty), and non-responsive to staining. The plugs lie in a fibrous stroma, here and there invaded by the cells. Nevertheless the tumor bears a certain microscopic similarity to squamous cell carcinoma, the more so, because concentrically arranged endothelial pearls also occur. There is no cornification or keratohyalin, or intercellular bridging, however. Fick considers psammomatous endotheliomas of the dura as epitheliomas belonging to the group of undifferentiated carcinomas (basal cell or corio-carcinoma), while Ribbert and Prym consider them endotheliomas—(see in opposition, Ricker-Schwalb).

(*e*) Parts of certain tumors of the salivary glands, (see p. 180, illust. V), are supposed to be derived from the endothelial lining of lymph spaces. The cells form networks consisting of branching cells often embedded in a fibrillar myxomatous, or hyalin ground substance, or they form clumps or strands of polymorphous, cubical and spindle-shaped small cells with a fluid or fibrillar interstitial substance. Frequently, the cell masses contain globular, peg-like, or cylindrical hyalin, or colloidal masses considered excretory products of the cells. In this way, glandular or ductal tubular structures appear as if filled with secretion. The cells may be flat, swollen, cuboid, cylindrical, radiating, etc., enhancing the resemblance to epithelial glandular structure. Sometimes large empty spaces with flat cells look like lymph spaces. Doubtless, however, most of these structures are of epithelial nature as in the so-called "mixed tumors of the parotids" (for details, see there), or hyalin endotheliomas (Klebs), or interfascicular endotheliomas (Ackermann), cylindromas, etc., formerly called sarcoma by some (ductal sarcoma, endothelioid angiosarcoma, Bizoz-

zero). We use the name cylindromatous lymphangiomatous endothelioma. The formation of hyalin cylindrical enclosures is so marked that they must be taken into consideration in the nomenclature. To call the tumor simply "cylindroma" is impossible, since there are also real sarcomas starting from blood vessels and showing hyalin cylindrical structures similar to those seen occasionally in both benign and malignant epithelial tumors. The author must agree with the present opinion that tubular and strand-like proliferations are epithelial (ectodermal) structures—this, on the basis of new experience in the majority of the so-called mixed tumors of the salivary glands (more under parotid).

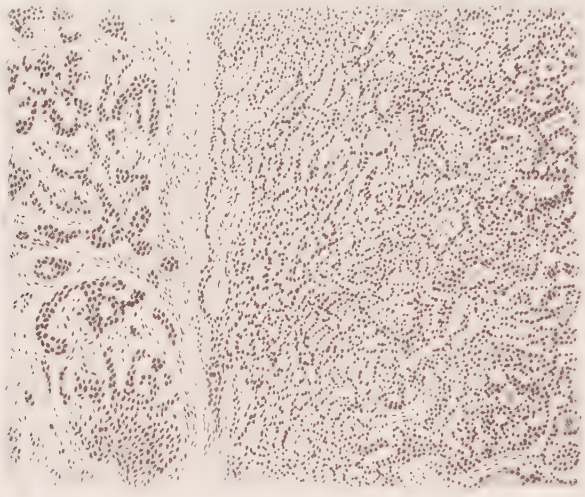


FIG. 104.—Basal cell carcinoma of palate; right portion cylindromatous (formerly called cylindromatous lymphangiomatous endothelioma), 70 year old woman (medium magn.).

(*f*) Tumors of structure similar to those mentioned under (*e*) occur elsewhere, as in the scalp (Haslund), face, cheeks, orbital region (see Barbezat, lit.), nose, and but rarely in other places as the arm (comp. Berti). Most of them, formerly called endotheliomas, must now be considered cylindromatous epitheliomas or carcinomas. Krompecher (lit.) calls them basal cell carcinomas (see also Coenen, Borrmann and Grawitz).

(*g*) Quite early, the so-called endotheliomas of the gums, (for details see there), were considered by Malassey as epithelial, and they really are, according to later investigations, cylindromatous basal cell carcinomas with a marked tendency to hyalin and mucoid degeneration within the epithelial strands and the connective tissue stroma (see fig. 104). As a whole, they are clinically benign.

(*h*) In reference to cellular naevi, which are only partially of endothelial nature, see under skin, -for so-called uterine endotheliomas, see there.

Histogenetically, endotheliomas belong to the connective tissue tumors, and in their structure are similar both to their typical representative, those poor in cells, and to the atypical, *i.e.*, the cellular sarcomas; which means that some are benign like fibromas, and most of the dural endotheliomas, and some are malignant like sarcomas which include many blood vessel endotheliomas as well as some endotheliomas of serous membranes. Nevertheless, "cellular" and "malignant" are not in themselves synonymous, and therefore cellular endotheliomas cannot be generally and simply called sarcomas, *i.e.*, endothelial sarcomas, to include the clinical conception of malignancy, because some endotheliomas, as in the meninges, may be very cellular and yet benign in their relationship. For this reason, in spite of the doubts of L. Burkhardt, the author would continue the formal separation of endothelioma from sarcoma in a histological sense. (Lit. by Monckeberg, Juliusberg, Krompecher, n. Hansemann, Marchand, Borst.)

**Distribution of Malignant Tumors by Way of the Lymphatics**

In contradistinction to the tumors which arise from the lymph vessels themselves as discussed in the preceding paragraphs, this concerns invading tumors which penetrate the lumena of lymph vessels and continue their growth in the preformed channel without any relation to its endothelial lining which disintegrates or may sometimes be seen on the outside of the carcinoma plugs, (see p. 18, fig. 4).

(*a*) Carcinomas. The dissemination of carcinoma frequently follows the course of lymph vessels, while sarcomas prefer blood vessels. This is exemplified in relation to regional infiltration of lymph nodes, *e.g.*, in mammary carcinoma, it appears in the axillary nodes. Similar examples may be given in other regions.

That carcinoma cells spread by preference, although not exclusively (see under veins, p. 167), by way of lymph spaces, is beautifully illustrated in the pleura when infiltrated through the thoracic wall by carcinoma from a mammary growth, or from a metastatic pulmonary nodule, or retrograde from an invasion of the bronchial nodes, *e.g.*, from the stomach. The lymph vessels may look like rosaries and be completely filled with white tumor masses which may also involve the intrapulmonary lymphatics. This is called carcinomatous lymphangitis, or better, lymph vessel carcinoma (details and illustrations under lung).

Secondary carcinoma of the thoracic duct is not unusual, (lit. by Winkler, Schwedenberg, Piot). The author himself observed cases, 6 in carcinoma of the bladder, 5 in gastric carcinoma, 6 in cervical and uterine carcinoma, 1 in ovarian carcinoma, and 1 in rectal carcinoma. The invasion may be of the intima, or of the whole wall and the tissues around

the wall, with focal or multiple stenoses; sometimes the duct is distended throughout its entire length to the thickness of a finger. Or the duct may be filled with tumor masses resembling a fatty cellular mushy admixture to the lymph. Notwithstanding marked infiltration of the duct, metastases to the lung may be absent. The supraclavicular nodes, particularly the left, more occasionally, the right alone (lit. by Hosch), or both, may be markedly infiltrated from a primary tumor far distant (as in the abdomen). This fact has clinical diagnostic value. Chylous hydrops almost never occurs. Details under metastatic tumors of the lungs.

Under pathological conditions, especially in the spread of some carcinomas, it is very impressive to see the intimate relation of apparently separated divisions of the lymphatic system. The established ideas of regional connection between lymph vessels and correlated nodes, and the experience of artificial injections are insufficient as explanations. These unusual relations are for the most part produced by retrograde transportation. Compare the special reports under mammary carcinoma.

(*b*) Lymphosarcomas in their spread often show a close relation to the lymph channels (see under lymph nodes).

(*c*) Enchondromas also occasionally invade the lymph channels, and as in C. O. Weber's case, the lymph nodes also.

(*d*) Sarcomas also (see under bones).

### Parasites

In reference to filaria sanguinis, see under blood (p. 210), and under elephantiasis (under skin).

## CHAPTER II

# BLOOD AND LYMPH. HEMATOPOIETIC ORGANS

### BLOOD

The pathological anatomy of the blood is of great clinical interest, but all the correlated details cannot be discussed here; the more important literature is given in the text and appendix.

See complete presentation of the pathology of blood by Paltauf, Freund, Sternberg. Textbook of General Pathology by Krehl, Marchand, II Vol., 1 sect. 1912; and Naglli, Blood Diseases and Blood Diagnosis; H. Hirschfeld, Textbook of Blood Diseases, Berlin, Hirschwald, 1918. Morphological hematology is exhaustively treated by H. Pappenheim and H. Hirschfeld, Hematological Tables, Leipzig, Klinkhardt, 1920.

#### Changes in the Quantity of Blood

The blood volume in adults, formerly calculated from animal experiments as $^1/_{13}$ of the body weight, has been estimated in man, according to modern methods, as between 7% and 8% of the body weight.

**Increase in Blood Volume.**—True plethora may result from abnormally rich alimentation or may appear in idiopathic cardiac hypertrophy (see p. 77).

Usually, the number of erythrocytes and the hemoglobin of the blood are increased, (see p. 187, for lit. of polycythemic plethora; also Senator, Hart and others).

**Decrease of Blood Volume.**—Oligemia or anemia appears immediately after massive hemorrhage as a purely quantitative change. When the blood regenerates after sudden loss via activity of the bone marrow, qualitative changes appear at once; the blood becomes relatively poorer in red cells because the fluid constituents are much more quickly replaced (oligocythemia).

Chronic anemias also are always accompanied by qualitative changes in the blood (see p. 189, etc.).

#### Changes in the Quality of the Blood

**Alteration of the Fluid Elements.**—In hydremia, water is retained in the blood, as in diseases of the kidneys, heart and liver. It is transitory in posthemorrhagic anemia. In anhydremia the blood loses part of the

water and salts, while the protein content changes but little. It becomes like tar, or thick huckleberry juice, as in cholera, etc.

In hypoalbuminosis, the blood is impoverished in proteins from increased protein consumption, or decreased supply, or both.

In hyperinosis, the plasma contains more of the fibrin-coagulating elements, and especially massive fibrin coagula are found in the cadaver in inflammatory diseases, especially pneumonia, and acute suppurations, also in the leukemias.

Hypoinosis, delayed coagulation, or decreased tendency thereto, presumably is due to decrease in fibrin ferment, *i.e.*, according to later opinion, to thrombogen. The blood shows delayed or lost coagulative ability when there is excess of carbonic acid, *i.e.*, $CO_2$, in the blood, as in asphyxia, poisoning by sewer gases, and cyanogen. In hemophilia, according to Petren, the coagulating ability is decreased, and the coagulation time increased.

Hemoglobinemia consists in the appearance in the blood of hemoglobin from dissolved erythrocytes. The serum is ruby red, or the color of varnish, instead of clear yellow. In a thin layer, blood is opaque, but if, as in hemoglobinemia, the hemoglobin is dissolved in the serum, it becomes transparent, and since only a small amount of light is reflected from within outward, the blood appears darker in a thick layer. If the spleen, liver and bone marrow are unable to completely metabolize the hemoglobin carried to them by the circulation, it enters first the bile (hemoglobinocholia, see Schurig), and then the urine (hemoglobinuria). In more marked hemoglobinemia, icterus may appear. Red blood cells which have lost their hemoglobin are called shadow cells (Ponfick). Hemoglobinemia is caused, among other things, by burns, freezing, cold (see Fox and Salin), transfusion of foreign blood (see Miller), various poisons, such as fungi, (see Boehm), glycerin, sulphuric acid, pyrogallic acid, toluendiamin, arsine, phenol, lysol, etc. Blackwater fever is not merely a hemoglobinuria, the urine becoming dark brown from the use of quinine, as R. Koch and Kleine supposed, but is an acute hemolytic malaria (see Plehn). According to Nocht, chemical influences are of importance in initiating isolated attacks, *i.e.*, hypersensitiveness to hemolysis from quinine, phenacetin, antipyrin, etc., (Ziemann, lit.).

**Changes in Blood Platelets and in Red and White Blood Cells.**—Blood platelets, first recognized by Bizozzero as the third structural element of the blood, are rounded bodies of light specific gravity, tenacious, and agglutinative, from 2 to 4 microns in diameter, and in numbers of 250,000 to 300,000 (Degwitz) per cubic millimeter of blood. Their number varies greatly, according to J. Bauer. They are factors in blood coagulation and thrombosis, and are therefore also called thrombocytes. Their

origin is still subject to controversy, but according to Wright's and Ogata's opinion which is generally accepted, they are separated pseudopodia from the protoplasm of the bone marrow giant cells (megacaryocytes). The number and appearance of blood platelets are parallel to that of the megacaryocytes as seen in pernicious anemia and lymphatic leukemia in which they are both absent or much decreased, while in chlorosis, (disputed), and in the hemorrhagic anemias and myeloid leukemia, both are increased. Bunting saw an increase of both in Hodgkin's disease. Arnold and Schwalbe think the blood platelets are derived from erythrocytes. Schilling thinks they are nuclear remains of erythrocytes. For other opinions, see Paltauf (lit.), Naegeli, (lit.), Brown, Downey, Hanser, (lit.), Cesaris-Demel, Kaznelson (lit.), Brieger and others. Lack of platelets is called thrombopenia. As to variation in their number, see Port and Akiyama (lit.), Duke (lit.). Used up platelets are destroyed, chiefly in the splenic pulp cells (Bernhardt).

**Changes in the Red Blood Corpuscles (Erythrocytes). Change in Their Numbers.**—Normally a cubic millimeter of blood in the female contains four and a half, in the male, five to five and a half millions of red blood cells (Vierordt). In pathological conditions, their number may sink to lower than one million; in leukemia to one-half million (oligocythemia).

Numerous red blood cells may be rapidly removed from the body or be destroyed in the blood. The former occurs in loss of blood, *e.g.*, in typhoid fever, the latter, after burns or chilling of the skin, in various so-called blood poisons, etc., (see above, under hemoglobinemia).

Oligocythemia is chronic in the hemorrhagic diatheses, malignant tumors, primary blood diseases (chlorosis, leukemia), chronic intoxications, (lead, mercury), infections, (syphilis, malaria); and without demonstrable cause in the so-called essential anemia, which, in progressive pernicious anemia, its most severe form, is fatal.

Polyglobulia, hyperglobulia or polycythemia is an increase of erythrocytes occasionally qualitatively changed. The count may reach eight, and even thirteen millions (Kulbs, Hirschfeld). It may be relative, *i.e.*, the blood thickens subsequent to loss of plasma, as in cholera, purgation, profuse sweats, polyuria, diabetes, etc., or absolute, due to erythroblastic hyperactivity (Turk), *i.e.*, increased erythropoesis in the bone marrow, (see exhaustive lit. *re* these and other theories by Jung); or it may be due to decrease of erythrolysis in the spleen and liver (Weintraud). Usually, absolute polycythemia goes with true plethora. There are (*a*) primary polycythemias (true red) or erythemias (compared to leukemia), developing from unknown causes (lit. by Jung, Herrnheiser); and (*b*) secondary polycythemias caused by various toxic substances such as phosphorus, arsenic, carbon monoxide, blood pressure increases (adrenalin, caffein).

They also appear in high altitudes, and in congestion of the pulmonary circulation, as in cardiac lesions, especially if congenital, in emphysema, in which the relative lack of oxygen is considered the primary factor (Kuhn, Mahr) in stimulating the bone marrow to increased erythropoesis. We might speak, with Hirschfeld, of erythrocytoses, in contrast to leukocytoses. The forms of erythremia are the Vaquez-Osler disease, (polycythemia, cyanosis, splenic tumor), and hypertonic erythremia (Geisbock), accompanied by increased blood pressure; the course is usually chronic and often ends by cerebral hemorrhage (see statistics by Clark Jones). At times, polycythemia is combined with myeloblastic leukemia (Jung, lit.). According to Hirschfeld, there are individuals who react after splenectomy with severe polycythemia (see Rendu and Widal, Sotti, R. Storn, lit., Paltauf, lit.; see also Engelkind who discusses polycythemia as a transmissable disturbance of the internal secretions).

**Changes in Shape.**—Erythrocytes containing granules, bodies and nuclei. The plane diameter of normal red blood corpuscles—although the dimensions vary greatly—is 7.5 microns, and their thickness is 1.6 microns. When abnormally small, they are called microcytes (microcytosis); when large, they are called megalo- or macrocytes. Deformed cells shaped like pears, handles, anvils, kidneys, sometimes even small fragments, are called poikilocytes (poikilocytosis—Quincke; see p. 200, illustr. I).

Basophilic stippling of erythrocytes consists of finer or coarser granules staining intensively with basic dyes (blue with methylene blue, Romanowsky stain; red with pyronin-methyl-green). It appears in the anemias, leukemias, polycythemia, and in lead poisoning; in the latter it is considered by many as of diagnostic importance.

Howell-Jolly-bodies are small round granules in the erythrocytes, usually appearing singly, sharply demarkated and intensively staining with hematoxylin, since they are nuclear remnants. They are found in the various anemias, and constantly, even for years, after splenectomy, (see Hirschfeld and Weinert, Roth, Karlbaum).

Blood dust or hemoconia (H. F. Muller) is partly composed of fat granules and is especially plentiful after fat ingestion (A. Neumann, Weitmann, lit.).

Erythroblasts are nucleated red blood corpuscles, *i.e.*, the mother cells of the erythrocytes circulating in the blood. They appear in the circulating blood in pernicious anemia, sometimes in other severe anemias, in metastatic carcinoma of the bone marrow, especially in carcinoma of the stomach, in myelogenous leukemia (see fig. 105; and p. 200, illustr. II). They are of normal size ("normoblasts," Ehrlich), or larger, (megaloblasts) fig. 105, and p. 200, illustr. II). Erythroblasts are physiologically found only in the blood-making organs. Newmann thought them

transition forms. Embryonal red blood cells are much richer in hemoglobin than adult cells (E. Meyer and Heineke). While megaloblasts are the chief cells in earliest embryonal life, they are replaced during further development by normoblasts, which, however, at birth, appear in but small numbers.

**Changes in Hemoglobin Content.**—In living normal blood, hemoglobin is the oxygen carrier as oxyhemoglobin. If blood is shaken in the air, gas-free hemoglobin reabsorbs oxygen. So, too, in autopsies, the fresh section surfaces of organs change from dark or bluish red, to a much lighter red because of the oxygen absorbed.

In the male, the hemoglobin content is 13% to 14%, *i.e.*, each 100 gms. of blood contains 13 to 14 gms. of hemoglobin. In the female, it is about 12.5%. In oligochromemia (diminished hemoglobin content) the percentage may drop to 6%, even to 3%. The blood becomes clear and watery. Oligochromemia may occur with a normal number of erythrocytes, or with oligocythemia.

In all conditions of chronic dyspnea, the hemoglobin content rises, (Naunyn, Weintraud, lit.), especially in erythremia (see p. 187). Clark-Jones found eight and one-half million red blood cells, and 110% hemoglobin in a case of Vaquez-Osler disease. For the greater hemoglobin content of embryonal erythrocytes, see above.

**Diseases Distinguished Especially by Qualitative and Quantitative Changes of the Red Blood Corpuscles.**—Chlorosis, or green sickness, appears in girls at puberty; it shows a decreased hemoglobin content, with many pale, so-called pessary forms of cells, (see fig. 105); poikilocytosis and a slight reduction in red blood cells which are large, and as a rule, pale in color, are also present. The etiology is unknown, but a disturbed endocrine balance between the ovaries and blood production is suspected. The function of the ovaries is said to be diminished, (Naegeli v. Noorden), and this is supposed to affect blood formation unfavorably, and so with the increased demands at the time of puberty, a pathological condition results. Increased blood destruction does not occur in this disease (Kahane, lit.). The increase of blood platelets which contain thrombokinase (Morawitz, more recently, by Fonio) may cause a tendency to thrombosis. (See especially under sinus of the dura mater.) For changes in the heart and vascular apparatus, see p. 71.

**Progressive Essential Anemia—Progressive Pernicious Anemia (Biermer).**—(In reference to Addison-Hunter as pioneers to Biermer, see Hannema and Josselyn deJong, Genees Kundige Bladen #9 u. 10 Harlem, de Erven F. Bohn 1921.)

The blood is thin, pale to amber yellow, and the coagulation power greatly diminished. The leucocytes as a whole are decreased in number,

especially the polymorphonuclears, while the lymphocytes are relatively increased (Lazarus); the blood platelets, the giant cells in the myeloblastic bone marrow, and especially the red blood cells are diminished. The latter are relatively rich in hemoglobin, are of varying sizes (micro- and megalocytes), and show poikilocytosis. Myelocytes appear in small numbers. The remarkable findings are the normoblasts and megaloblasts (Schridde's primary erythroblasts), which appear in varying numbers (see fig. 105) and are found in equal quantity in the bone marrow. This latter, according to Ehrlich's theory of the cause of pernicious anemia, is chemically irritated, and the type of reaction is pathological and purposeless. Another theory ascribes the primary factor to a toxic blood destruction (comp. E. Meyer a. Heineke; p. 191). The megaloblasts, as well as used up and altered erythrocytes, become the prey of endothelial and other phagocytes in the "hemolytic" and, at the same time, "hematopoietic" organs, *i.e.*, the lymph nodes, spleen, and bone marrow (see Gulland and Goddall). Pernicious anemia is also called "megaloblastic anemia" by those who consider the megaloblasts as characteristic of the disease (see Bloch, and in opposition, E. Meyer a. Heineke). The nature of the disease consists of a progressive impoverishment of the blood in erythrocytes and hemoglobin. Etiologically, the differentiation is made of (*a*) cryptogenetic primary pernicious anemia, called also Biermer's anemia. Most cases are of this type and end in death, usually in one to two years, or later, when interrupted by remissions. Practically only adults are affected. (*b*) The second type is composed of isolated cases with known causes, which, however, correspond otherwise with type (*a*), (Schaumann and others). One of the most important of type *b* are the occasional anemias caused by bothriocephalus (Tallquist, T. and Faust), and by taenia saginata, ascaris or ankylostoma (see Preti). These parasites produce hemolysing toxins. Removal of the parasites leads to cure of the anemia. Others consider that non-specific gastrointestinal disturbances may also be responsible. They suspect autointoxication from hemolysing products of increased intestinal decomposition (Grawitz). Gastritis, achylia and absence of hydrochloric acid production allow increase of growth of intestinal hemolytic bacteria (Faber). Seyderhelm studying in animals the activities of the bacterial poisons contained in the intestines, produced grave hemolytic anemia by the introduction of fecal toxins, not per os, but directly into the bowel, thus obtaining a reaction in this respect like that of the toxins of the animal parasites mentioned. Other causes considered are: pregnancy, the puerperium (rare), carcinoma of the bone marrow, syphilis, malaria, and other infectious diseases, malignant osteomyelitis, (lit. by W. Hunter and Bunting), certain poisons, arsine, nitrobenzol. These diseases, however, which differ also in their blood picture

from true pernicious anemia, belong for the most part to the symptomatic anemias (Turk).

**Translator's Remarks.**—The remarkable remissions in pernicious anemia observed on feeding liver have led to the thought that the disease may have a dietary basis, but a study of the pre-disease diets of patients with pernicious anemia showed nothing remarkable. Cornell. B. S.; Bull. J. Hopkins Hosp., 40, 409, 1927.

The striking findings in the cadaver are the pallor and the fatty degeneration of various organs such as the heart and liver (central fatty degeneration). The epithelium of the stomach and intestines, the kidneys and pancreas, is also degenerated; the gastrointestinal mucosa is atrophic and shows small cell infiltration considered by some as inflammatory (see Herzberg). The liver is pale, sometimes rust colored or brownish red from hemosiderin deposits. This disintegration product of erythrocytes is found also in the moderately enlarged spleen, the bone marrow and the kidneys (their sclerosis by Paszkiewicz). Hemorrhages in various organs can almost always be found and are most remarkable in the serous membranes, especially the pericardium beneath the endocardium, in the meninges, background of the eye, brain and spinal cord which may also show foci of degeneration (Camac and Milne, lit.; Lenel, Richter, Brouwer, Blawknipp). The bone marrow is rich in erythroblasts, among which the megaloblasts and megalocytes predominate; there are also myeloblasts, while the cells of the type of granulocytes diminish, and usually there is a relative lymphocytosis.

Extramedullary blood-forming foci are of special interest in the pulp of the spleen (the lymphoid part is crushed), in the liver (intraacinous and periportal), and, more rarely, in the lymph nodes (E. Meyer and Heineke, Nicol). The so-called myeloid change occurs (Dominici), *i.e.*, the formation of foci of young leucocytes, myelocytes, and forms of erythroblasts which may enter the blood. This is interpreted as a useful attempt at compensation in the face of a primary blood injury.

Myeloid metaplasia, also called extramedullary myeloid tissue formation, occurs not only in the spleen, liver, etc., but in all sorts of places, such as autochthonous, from indifferent perivascular connective tissue cells (lit. by Naegeli). And it also appears in extensive destructive processes of the bone marrow as in carcinoma, various infections, (pneumonia, scarlet fever, etc.), as well as in anemias (phlebotomy, septic anemias, post-hemorrhagic, toxic-experimental and childhood anemias); also in certain cases of congenital dropsy (see under spleen, p. 241); (lit. by Werzberg, and compare with chronic myeloid leukemia, p. 201). [Lit. D. Brannan, Bull. J. Hop. Hosp., 41, 104, 1927.—*Translator.*]

In congenital hemolytic anemia, also called familial icterus, (Minkowsky), or familial hemolytic icterus (according to Meulengracht, lit., it is truly hereditary) with splenomegaly, there is an hereditarily altered structure of the erythrocytes which dominates the picture (Widal). Among its physical and morphological changes appears diminished osmotic resistance, *i.e.*, considerable lessening of resistance to hypotonic saline solutions. The next most characteristic sign is anisocytosis (Chauffard), with remarkably small, but thick and more globular cells. Polychromatophilia is also seen as a grayish blue color with Giemsa stain. The large, spodogenous (Ponfick), vascular, splenic tumor shows no connective tissue increase, (histology by Guizetti, Graf, Kleeblatt); it contains pigment, some iron-bearing and some not; the latter is also found in the liver and

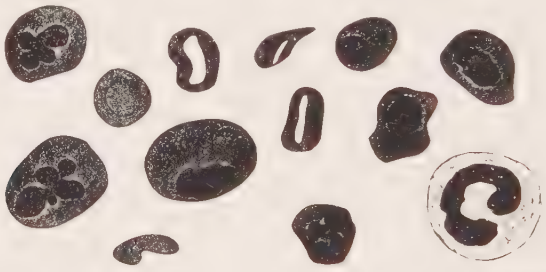


FIG. 105.—Megaloblasts and poikilocytes (incl. pessary forms); below-right, a leucocyte; blood of secondary pernicious anemia, 40 year old man with carcinoma of stomach and numerous variegated metastases in the skeleton; large pulpy spleen.

kidneys. Otherwise the liver and bile ducts show no changes. The bone marrow is red and bloody, and regeneration is shown by erythrocytes with basophilic granules and with nuclei.

The genesis of the icterus is not clear, but Widal considers it truly hematogenous. The blood serum is dark yellowish brown from bile pigments. The patients never have bradycardia, pruritus, nor acholic stools; in fact, the stools are rich in bile pigment, nor is there bile pigment in the urine, (acholuric icterus), but urobilin is almost always present, (see also Lepehne, as to the pathogenesis of icterus). Anemia is usually moderate, becoming more severe during the crises. The prognosis is not bad. Splenectomy at times gives good results (Banti, see of the failures, Gerhardt); but the lowered osmotic resistance of the erythrocytes does not disappear (Roth, lit.; Naegeli, lit.). For experiments on the action of hemolytic sera, see Bonome.

**Translator's Remarks.**— Bile pigment is frequently present in the blood in pernicious anemia, but it differs in being "fixed" to the plasma, and not appearing in the urine or definitely in the skin. It is said to be hepatic in origin. See Blankenhorn, M. A., Arch. Int. Med., 19, 344, 1917.

The rare, so-called aplastic or aregenerative anemia does not represent a new uniform etiological group since it is met as the final stage of severe simple, or pernicious anemia, and as a possible sequel of infections, (staphylococcus sepsis, gonorrhea, see Buschke and Hirschfeld), or of x-ray injury to the bone marrow (see experiments of Heineke, leucopenia), and of severe intoxications (benzol, arsenbenzol, see Gorke, lit.). It is an expression of exhaustion of the hematopoietic organs, especially the bone marrow. There is a thrombopenia, (see p. 186); the characteristic myeloblastic reaction is absent, and in the organs mentioned above, there are no blood-forming foci. Erythroblasts as well as megalocytes are absent. The number of leucocytes is usually very low (leucopenia). As in pernicious anemia, there are hemorrhages and fatty degeneration of the parenchymatous organs; for this reason, aplastic anemia is also called aleucia hemorrhagica (E. Frank). See under bone marrow in reference to experiments on this question.

Anemia pseudoleukemia infantum is secondary to various causes (syphilis, rachitis ?, alimentary injuries, etc.) (Naegeli) in which there is marked functioning of the erythropoietic and leukopoietic parts of the blood forming organs (erythroblastosis, leucocytosis). Myeloid tissue formation may induce great enlargement of the spleen and liver, and Tanaka observed it in the connective tissue of the renal hilum. The blood picture shows a grave anemia, *i.e.*, decrease of erythrocytes and hemoglobin, with normoblasts, megaloblasts, and marked leucocytosis. According to Naegeli, it is a biological variation of any form of a secondary anemia, but only possible during the first months of life. It is advisable to discontinue the designation "splenic anemia" for this and other forms of secondary anemia combined with splenomegaly (see p. 226).

In the leukemia described first by Leube-Arneth, the pernicious anemia blood picture is added; without exceptional increase of leucocytes, their relative percentage is so altered that the myelocytes and the small lymphocytes are much increased, while the percentage of the polymorphonuclear neutrophiles is decreased, (in the case of Leube to 43.9%).

Its exact position in classification is undecided, whether acute leukemia with more marked accompanying anemia, or whether severe anemia, atypical anemia (Naegeli), or a combination of leukemia and hemolytic anemia (lit. by von Domarus, Masing, Martelli and others).

**Translator's Remarks.**—So-called sickle cell anemia first described by Herrick (Arch. Int. Med., 6, 517, 1910) seems to be a definite disease entity occurring only in the negro, in whom there is apparently a fundamental racial disposition. Its characteristic is the sickle shape of the red cells which, however, according to

Josephs (Bull. J. Hop. Hosp., 40, 77, 1927) disappears on washing to be resumed when the cells are resuspended in their serum. Perhaps some substance adsorbed causes the change in shape. The characteristic shape may be present, however, without anemia and be discovered in routine examinations of negroes by suspending their blood and examining it thus. It seems to be familial in distribution, but over widespread geographic areas. Autopsy studies thus far are too few for definite conclusions, except that it is probably an hemolytic anemia. See Graham, G. S., Arch. Int. Med., 34, 778, 1924.

**Changes of Leucocytes.**—The proportion of white to red blood cells is normally 1 to 300 or 400, or according to others, 1 to 335 to 600 (5500–8000 per cmm.). The leucocytes (a term including the white blood cells as a whole) are classified according to form and number of nuclei, or according to the staining quality of the protoplasm and the granules contained within. They are divided into (Lowit, Ehrlich, Naegeli, Schritte):

(1) Lymphocytic cells with simple rounded or oval nuclei, basophilic protoplasm, and so-called Altmann granules. Their sources are lymph nodes, splenic follicles, and the lymphatic tissue, mostly perivascular in almost all organs. They are capable of immi- and emigration, and according to Bergel, are phagocytic to fat.

To stain Altmann granules, the material should be as fresh as possible; it is fixed in chrome-osmic acid; paraffin sections are attached to slides and stained in 20% aniline water acid fuchsin, and differentiated in alcoholic solution of picric acid. The granules stain red (fuchsinophile).

To the group of lymphocytic cells belong:

(*a*) Lymphocytes, (small), which are approximately the size of a red blood corpuscle with small round nucleus rich in chromatin, and little protoplasm; these make up about 20% to 25% of the white blood cells.

(*b*) Lymphoblasts, large lymphocytes, 1.5 to 2 times as large as (*a*), have larger oval nuclei, and are less rich in chromatin. They are mother cells of (*a*) and are normally found in the germinal centers of lymph nodes, 6% to 8% in the blood.

(*c*) Plasma cells (see p. 9) are almost always found in tissues, and but rarely in the blood.

(2) Leucocytic cells possess, when mature, a polymorphous nucleus, rich in chromatin, with acidophile protoplasm and the so-called Ehrlich's granules. They are formed in the bone marrow.

To demonstrate Ehrlich's granules, use Ehrlich's triacid stain, consisting of a mixture of solutions of orange b, acid fuchsin, and methyl

green. According to their staining qualities they are differentiated into neutrophilic granules which stain violet, and eosinophilic granules (or acido- or oxyphilic) which stain red. Some granules stain with the basic dyes, *i.e.*, acetic acid, rosaniline, dahlia, methyl violet, gentian violet, fuchsin. These are called basophilic granules.

To the group of leucocytic cells belong:

(*a*) Myeloblasts (Naegeli), which are plump, oval cells with large, oval, light nuclei, and medium basophilic protoplasm surrounding the nucleus. They have no granules, at least in sections, while in smears, fuchsinophile structures are demonstrable (comp. Butterfield, Heineke, E. Meyer and Naegeli). They are the mother cells of all the others belonging to this group, inclusive of the polymorphonuclear leukocytes. They are developed in the embryonal myeloid tissue of the liver, and of the spleen, and in the bone marrow; in the latter they are more abundant in children than in adults. The bone marrow giant cells are also supposed to originate from myeloblasts (see Naegeli). They enter the blood in numbers only under pathological conditions, as in infectious diseases, burns, in hyperactivity of the myeloid system, particularly in myelosis and polycythemia (see p. 286).

(*b*) Neutrophilic myelocytes have nuclei like (*a*); the protoplasm is slightly acidophilic, with neutrophilic granules. They are abundant in the bone marrow.

(*c*) Eosinophilic myelocytes, and

(*d*) Basophilic myelocytes differ only in their granules; otherwise they are like (*b*). They are sparse in the bone marrow.

(*e*) Neutrophilic polymorphonuclear leucocytes (the so-called polynuclear leucocytes) have three or four nuclear fragments held together by delicate chromatin bridges, and possess very fine granules showing with neutral stains, (methyl green-methylene blue and staining acid, acid fuchsin). They constitute the bulk—about 70%—of the white blood corpuscles (4500 per cmm.). They are the most important microphages in infectious diseases.

(*f*) Eosinophiles are polymorphonuclear leucocytes, (eosinophile cells), which take an acid granule stain, especially eosin. They are somewhat larger than (*e*). The nucleus is less lobulated. The normal blood shows 2% to 4% of these leucocytes.

(*g*) Basophilic leucocytes, or the so-called mast cells, are rounded bodies containing granules in their protoplasm which stain very intense with basic dyes (see above). The mast cells of the blood give the oxidase reaction, but the histiogenic mast cells, which are found in granulation tissue, (see p. 9), do not give this reaction; their mother cells are thought

to be lymphocytes embedded in perivascular tissue, (lit. Schridde), or according to Verratti (lit.), Marchand's adventitia cells, or cells similar to the clasmatocytes of Maximow (see also Greggio lit.). They constitute about 0.5% of the leucocytes, *i.e.*, approximately 50 per cmm.

(*h*) Large mononuclears or monocytes, about 18 microns in diameter, are the largest cells of normal blood, and have large, simple, pale nuclei. They are frequently active as macrophages, and with the so-called transition forms (more lobulated nuclei) constitute 6% to 8% of leucocytes (Naegeli). Their origin is disputed, but is surely not from one source. Naegeli believes they have separate granules, but belonging to the myelocytic granules; they give the oxidase reaction. Others think they are derived from lymphoid cells, or from splenocytes, or from adventitia cells (see the criticism of Naegeli, lit.). Kiyono thinks most macrophages are histiocytes formed by the rounding off and detachment of reticulo-endothelial cells of the spleen, lymph nodes, bone marrow, Kupffer's cells in the liver, and endothelium from the adrenals (see Schilling).

The cells discussed under 2, *a-b-c-d*, (p. 195), appear in the blood only in pathological conditions. Worn out leucocytes are eliminated in lymph nodes, spleen, and bone marrow.

The cells of the lymphocytic and leucocytic groups are sharply differentiated by the presence or absence of the Altmann or Ehrlich granules. Their origin varies, and thus far, no general mother cell has been found for both. Other differences are that only the Ehrlich granules give the oxidase reaction, *i.e.*, they stain blue after treatment with a-naphthol and dimethyl-p-phenylendiamin (Winkler). This reaction can be carried out on formalin frozen sections (W. H. Schultze). It is also spoken of as the indophenol blue-synthesis.

Oxidase reaction: Small pieces of organs, or better, parallel knife sections, *i.e.*, formalin frozen sections, are first placed for 3 minutes in a 1% alkaline aqueous solution of a-naphthol, then for the same length of time in 1% aqueous solution of dimethyl-para-phenylendiamin, are washed in water, and examined in water or glycerin gelatine. The solutions should ripen for 2 days and should not be older than 8 days (Rautmann). Leucocytic and myeloid tissue stains blue; lymphocytic tissue does not. Microscopic examination shows that all granular leucocytes have blue granules in the protoplasm. Lymphocytes do not stain (details by W. H. Schultze, lit., also Dunn). Methods of oxidase reaction for paraffin celloidin and gelatin sections by Strassmann, Fursenko, Winkler, Graff, v. Gierke and others.

In the dioxiphenylalanin reaction (so-called Dopa reaction of Bloch) the granules of the myeloid system stain black; nuclear and protoplasmic stains may be used later (see Matsunaga).

Ehrlich's classification of leucocytes depends on the assumption of specificity of the granules, but it has been stated (Arnold, Hesse, lit.) that the reaction may change in the same type of cell. Minkowski also has mentioned this, while Askanazy, Schridde, Naegeli and others energetically support the opinion of Ehrlich. (Lit. in reference to leucocytes by Naegeli and in appendix.)

**Changes in the Number of Leucocytes in the Blood.**—Leucocytosis is an increase in number of leucocytes—often transient—and in contradistinction to leukemia, of mature cells. Leucocytosis is a function of the bone marrow, although the existence of a true myelogenous leucocytosis is denied by Graff who supports the so-called displacement theory, *i.e.*, there is displacement of leucocytes in the blood and this causes the great differences in number between a peripheral and a cardiac count.

The usual type of leucocytosis, according to Ehrlich and Lazarus, is the polynuclear neutrophilic. To it belong the physiological forms, that of the new born, muscular exertion (see Becher), digestion, baths, pregnancy, and the forms in pathological processes, the infectious, toxic (*e.g.*, after therapeutic injections of collargol), anemic, (posthemorrhagic), cachectic, and starvation. During digestion, the proportion of leucocytes may be increased one to a hundred. Among infectious leucocytoses must be remembered that of pneumonia (v. Limbeck), of surgical suppurations (Curschmann, Kuttner), of early typhoid fever (Naegeli and others, see Kuhn, lit.; leukopenia appears still earlier in typhoid, see below). Polynuclear neutrophilic leucocytosis is considered, according to Ehrlich, a function of the bone marrow.

Some conditions which cause ordinary leucocytosis, especially infections, lead to the entrance of immature leucocytes (myelocytes etc.) into the blood (Schindler, lit.).

Eosinophilic leucocytosis (lit. by Schwarz) is found in asthma (see under bronchi), eczema, pemphigus, urticaria and other skin diseases, helminthiasis (ascaris, oxyuris, ankylostoma), trichiniasis (of diagnostic value, Schleip, see under muscles), the exudative diathesis (see Kroll-Lifschutz), mucous colitis, certain infections (especially scarlet fever), rupture of echinococcus cysts in the abdomen (Barling-Welsch), and sometimes in malignant tumors (Reinbach, Noesske), finally, although not constantly, after splenectomy. See experiments in relation to foreign proteins by Schlecht, and by Schlecht and Schwenker.

Local eosinophilia (histio-eosinophilia) or the collection of eosinophiles in tissue, occurs physiologically in the bowel, is frequent under pathological conditions such as lympho-granulomatosis or Hodgkin's disease (see there), around trichinae, around the bronchi in asthma, in the interstitial

tissue in skin carcinomas, intestinal carcinoma (see Oehler), etc., (lit. by Schwarz Goldzieher, Sternberg, Barbano, lit., Ayoyama).

Leucocytosis, as formulated by Askanazy, is a useful reaction usually to toxic-chemical irritations and consists of an essentially active invasion of increased quantities of leucocytes from the normally stored or increased supply in the blood-forming apparatus, *i.e.*, particularly the bone marrow. Lit. as to leucocytes by Helly.

Leucopenia—decrease of leucocytes—appears in the very beginning of typhoid fever; it is important in relation to appendicitis when there has been leucocytosis, in measles, severe anemias (see there). It is of interest that it also appears after the ingestion of benzol (lit. by Veit).

According to Naegeli, lymphocytosis is a reaction of the lymphatic apparatus mostly after a previous infectious or toxic injury which first caused a decrease of leucocytes. This is observed during the course of numerous intoxications and infections, after serum injections and in toxic goiter (lit. Helly). Moewes interprets chronic lymphocytosis as a condition of reaction and a sign of constitutional inferiority.

Lymphopenia—decrease of lymphocytes—is seen when the lymphatic apparatus has been injured by toxins, infections, or has been extensively destroyed by carcinoma, tuberculosis, etc.

Myelocytosis may appear in children with infectious diseases which cause grave functional injuries to the blood-forming organs; the myeloid system floods the circulation with immature marrow cells (comp. Jungmann and Grosser).

In leukemia, (Virchow) (see p. 200, illust. V, VI, VII), the increase of white blood corpuscles is permanent and progressive and finally ends in an oligocythemia in which the white blood corpuscles may outnumber the red. Immature forms also appear, mostly myelocytes (as in myelosis), more numerous than they are ever found in leucocytosis, although in the latter, a few myelocytes may be present (Engel, Turk). The leucocytic picture is also qualitatively changed. Finally, the absolute number of erythrocytes decreases (lit. to 1919 by v. Domarus and in appendix to pp. 195 to 197).

In advanced leukemia, the blood is a thin fluid, its specific gravity is reduced from 1.055 to 1.040 or 1.030, it is light red, as though mixed with pus or fat. Clots in the cadaver are light yellow to yellowish green, like bacon rind but softer, or white and smeary like cream. The duration of this practically incurable disease is usually some years; in the lymphatic form it may occasionally extend eight to ten years. Death occurs from anemia and cachexia, frequently with hemorrhagic manifestations. On the other hand, the author has seen forms running an acute course of only a few weeks. For x-ray treatment, see Martelli; for benzol therapy, see lit. by Veit.

According to Ehrlich, leukemia must be classified by the blood findings into two main forms, the lymphatic and the myelogenous. In the former, the blood findings are characterized by lymphoid cells, in the latter by myelocytes. The leukemic blood condition, however, is not the essential part of the disease, but only a symptom of a previously generalized systemic disease appearing in the total lymphatic-hemopoietic system and not in a primary focus; it is caused by an unknown noxa. To this noxa, every tissue reacts in a different way, but with unlimited hyperplastic proliferation, now lymphadenoid where the organs with lymphatic structure are first involved, now myelogenous, with myeloid tissue proliferation not in the bone marrow alone, but in many other organs such as the spleen, lymph nodes, liver, kidneys, etc., and the loose connective tissue. These tissue hyperplasias then supply the blood with cells which characterize the form of leukemia. The lymphatic and myelogenous forms are now frequently called leukemic lymphadenosis and leukemic myelosis respectively.

Mixed leukemias are extremely rare. Combinations of both forms, according to Naegeli (lit.), are developed by vicarious myeloid contrareactions, especially of the spleen (see Herxheimer also). It is not believed that transition of one form into the other is possible (see Naegeli).

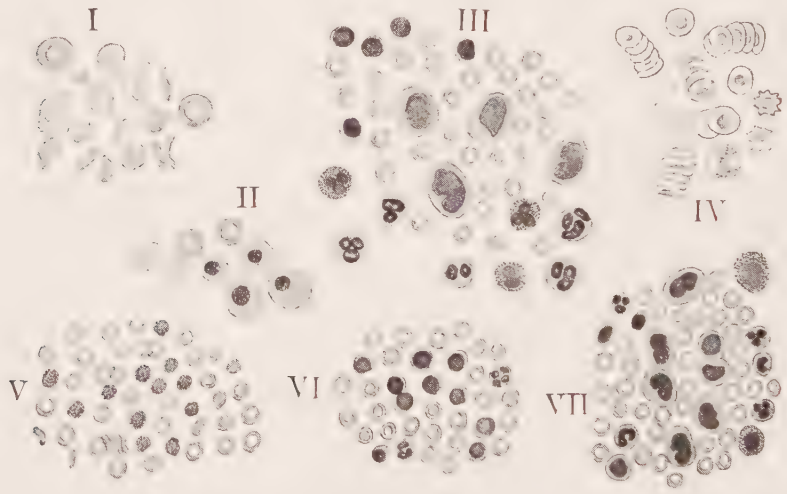
In leukemia, a remarkable volume increase of various organs frequently takes place as they participate in the increased leucopoiesis. Chief among them are the spleen (almost without exception), the lymph nodes, (quite frequently), and the liver. The bone marrow often, although not always, takes part; E. Neumann believes it plays a dominant role, but his view is not recognized by certain others. Formerly, three forms of leukemia were distinguished according to the predominance of one or the other, splenic, lymphatic, and medullary, (also splenomedullary). This classification has been abandoned, principally through Ehrlich's studies, and the type is now decided by the blood picture alone, *i.e.*, lymphatic, or myelogenous, and by the course, chronic, or (more rarely) acute. We shall discuss certain differences in the broad anatomical picture in the various chief types of leukemia such as more pronounced swelling of lymph nodes in chronic lymphatic, and the large splenic tumor in the splenomyelogenous form.

The two forms of chronic leukemia show two corresponding types of cells in the blood.

In the lymphatic type, the lymphocytes predominate. Their source is the lymphatic tissues which are enormously proliferated. These include the lymph nodes, the lymphadenoid tissue of the spleen, and the bone marrow, the latter considered especially responsible by followers of Neumann's theory (Kelly, lit.). The myeloid tissue of the marrow

becomes displaced by lymphoid tissue, thus explaining the uniform lymphocytic picture.

Sometimes the thymus is greatly enlarged. Invasion of lymphocytes into lymph channels and veins is observed (comp. p. 206, see also Nakamura). According to Ehrlich, lymphocytes are characteristic of the lymphatic form of leukemia which may also be called lymphadenoid leukemia, or according to the blood picture, lymphemia. The acute form may indeed be very rapid (few weeks), and the masses often invade the neighboring tissues with a tumor-like aggressiveness. The chronic form is characterized by ordinary small lymphocytes in excessive numbers, fre-




FIGS. 106–112.—I. Poikilocytosis. II. Various kinds of red blood corpuscles (hematoxylin-eosin stain); two normal (above); two shadow cells (left); one normoblast with deep blue stained nucleus (body intensively red); three megaloblasts (right) stained similarly. III. Various forms of leucocytes (red blood cells scattered between); above left, small mononuclear lymphocytes (nucleus deep blue); below right and left, polynuclear leucocytes (nucleus blue); to the right, below, two polynuclear leucocytes (nucleus blue) with eosinophilic (red) granules, eosinophiles. Of the four largest cells, the two lower with lobulated nuclei (pale blue) are so-called transition forms, the upper cells are large mononuclears-triacid stain. IV. Blood undiluted; rouleaux formation of erythrocytes; two thorn-apple shaped reds; a delicate granulated leucocyte with two nuclei; eleven blood platelets. V. Lymphatic leucemia, unstained. Leucocytes darker and granular. VI. Lymphatic leucemia, hematoxylin-eosin stain. Nuclei of leucocytes blue, body pale blue violet; below to left, nucleated erythrocyte (nucleus deep blue, body red) upper right, polynuclear leucocyte. VII. Myeloid leucemia (myelemia), hematoxylin-eosin stain; left, above, red blood corpuscle with eccentric deep blue nucleus, also a polynuclear leucocyte (nucleus deep blue); in center, large mononuclear myelocytes (nucleus blue, cytoplasm, pale blue); above to right, an eosinophilic, large mononuclear marrow cell; right below, eosinophilic, polymorphonuclear cell of nonleucemic blood.

quently with certain modifications especially in size; they may finally displace all other leucocytes. In the acute type, the more typical cell is she large lymphocyte with lymphoblasts. It is in the chronic form that the hyperplastic proliferation of the tissues producing these lymphocytes it especially marked, so that it is not difficult to form a conception of

lymphatic leukemia as a disease of the general lymphatic system (see also leukemic infiltrations, p. 203).

The second type of leukemia is the chronic medullary or myelogenous form, or myelemia (according to the blood picture), in which cells foreign to normal blood, chiefly myelocytes (see p. 195), are found. This is far more frequent than lymphatic leukemia. But other types of granular cells which are rare in normal blood also appear in abundance, such as eosinophiles, basophiles (mast cells), and myeloblasts (see p. 195, 2a), the number of which is characteristic in acute myeloid leukemia; various atypical (dwarf) forms are also found.

Mitosis is seen, and normo- and megaloblasts are present in considerable numbers so that the name "mixed cell" (Pappenheim, Grawitz) is not unwarranted. "Mixed leukemia," however, is entirely different; by it we mean a combination of lymphatic and myeloid leukemia (Herz), a condition which most authors believe does not occur; they consider the addition of myeloid proliferation to lymphatic leukemia a vicarious process, especially produced by encroachment on the myeloid tissue in the bone marrow (see p. 199). The earlier idea considerd the bone marrow the principal source of myeloid cells which might reach the blood corresponding to the normal post embryonal condition, but through the investigations of Dominici, Frese and others, it is now known that in the splenic pulp which is always enormously proliferated, and sometimes in the interfollicular tissue of lymph nodes, as well as in every other possible place (liver, kidneys, adrenals, pancreas and in connective and fatty tissue, etc.), myeloid cells arise from an autochthonous myeloid transformation (metaplasia) (Turk, Walz, Pinkus, Pappenheim and others). Thus myeloid cells may be produced in all these places; indeed, there have been cases of myeloid leukemia reported in which the bone marrow itself did not participate. It is therefore a general systemic disease of the hemopoietic tissue, and the bone marrow has no specific share in the total picture, even though its myeloid hyperplasia is important in the average case. This almost ubiquitous appearance of blood-forming foci represents a recrudescence of the hemopoietic activity, (Paltauf), which these organs and tissues displayed in embryonal time. M. B. Schmidt and Schridde believe the cells of capillaries are the originators of myeloid cells (myeloblasts, myelocytes, giant cells). According to Schridde, endothelial cells which remained undifferentiated, or fully differentiated cells which resume their undifferentiated form by direct metaplasia, regain developmental potentialities, of the embryonal primary cell. (For other theories, see Maximow, lit., Marchand.) Since the vessel wall cell is also the mother cell of erythrocytes, the appearance of normo- and megaloblasts is explained. But in leukemia, the direction of differentiation is one-sided, and principally

leucocytic elements are produced. Other workers assume that myeloid tissue is carried metastatically into these organs (metastatic-colonization theory), but Walz, Pinkus, Wolff and many others, have actively disputed the metastasis theory; this doctrine has few supporters (lit. by v. Domarus). Sternberg admits both possibilities. Comp. H. Fischer, Askanazy, and new experimental additions to the knowledge of extramedullary blood formation and lit. by Werzberg and Jaffe.

The acute leukemias (see p. 205, and lit. there) require further discussion. Clinically, it is often an acute, highly febrile disease with a severe hemorrhagic diathesis (see p. 205). The splenic tumor is usually less evident than in chronic leukemia, and this holds true of lymph node enlargement also; in fact, the latter may be entirely absent (etiology on p. 205). There are two forms. In (*a*) the lymphatic form, the common small lymphocytes may predominate, but this is rather unusual, and the post mortem findings do not differ from those of chronic lymphatic leukemia. Usually the blood shows a large mononuclear, non-granular round cell with delicately constructed, round, or kidney-shaped nucleus (Rieder forms), and a more or less narrow rim of cytoplasm. Cases are not rare —far more of them than of *b*—which are distinguished by a local, aggressive, infiltrating growth, and by extensive, voluminous, heterotopic proliferations, which give the condition a more tumor-like (lymphosarcoma-like) appearance, *e.g.*, in the neck, in the mediastinum, or in the various organs. Young individuals are preferred. Formerly, all large cell leukemias in Ehrlich's sense were considered large cell lymphatic, *i.e.*, according to the statements of Pappenheim, Hirschfeld, the proliferation of lymphadenoid tissue is so precipitate that the cells remain immature large lymphocytes (lymphoblasts). But now the majority of such cases are recognized as (*b*) acute myeloblastic leukemia (W. H. Schultze; Veszpremi, K. Ziegler, and others; lit. by v. Domarus, Klieneberger). The myeloid tissues are in too active proliferation and the cells are primitive myeloblasts, (see p. 195, 2a), but occasionally, even in the most acute cases, fully mature granular myelocytes may predominate (J. L. Burchhardt, lit.). Comp. under chloroma, p. 272.

The difficulty in distinguishing myeloblasts and large lymphocytes is sometimes insuperable, and differentiation by means of the blood picture may be impossible (Pappenheim, also Butterfield). We cannot continue this hematologic controversy, so we emphasize two points: first, the histologic findings. If, for example, we find atrophy by substitution in the lymphadenoid tissue of the spleen, the case is not lymphatic leukemia, but myeloblastic; if, on the other hand, we find so much hyperplasia in the follicles (without recognizing their actual germinal centres) that they are confluent and there is substitution of pulp by lymphadenoid tissue, then

the case is lymphatic. Secondly, the oxidase reaction (p. 196) assists in deciding whether the cells are lymphocytic or leucocytic (W. H. Schultze, Peters, Bingel-Betke).

Sternberg (see also Helly) would class as leucosarcomatosis, the acute large cell forms with tumor-like growths, local aggressive development and "metastases," especially in the kidneys; thus he separates them from the lymphatic leukemias, since the latter do not present true hyperplasia, but are more closely related to lymphosarcomatosis.

Many investigators, however, have opposed this view. They point out that occasionally small cell lymphatic cases show infiltrating aggressive tumor-like types of growth (Turk, v. Domarus), while large cell forms may run their course without tumor formation; moreover, there are cases in which large and small lymphocytes appear in the blood in equal numbers (lit. by Fabian, v. Domarus, Lehndorff, Herz).

Sternberg's cases probably belong to the large cell leukemias, partly lymphatic, *i.e.*, lymphoblastic (*a*), and partly myeloblastic (see Graetz, Pappenheim, v. Domerus, Naegeli, Eug. Fraenkel). (*b*) The examination of the cells for proteolytic ferments, which were demonstrated in those of myeloid leukemia by Jochmann and Muller, and especially the oxidase reaction, may help to decide whether a given case belongs to this or to the lymphoblastic form. In this way W. H. Schultze proved conclusively the myeloblastic nature of the large cells in his well known case which presented the picture of Sternberg's leucosarcomatosis. Sternberg thinks, on the other hand, it is entirely unjustifiable to class the so-called myeloblastic leukemia, which is nothing but a septic infection, with myelosis, *i.e.*, among the true leukemias (see Paltauf, and opposed, Steffan and others).

New formation and replacement of the erythrocytes are disturbed, so that they decrease in numbers. The diminution of hemoglobin content and the dependent iron content of the blood run parallel. Sometimes poikilocytosis is seen; normoblasts were mentioned above.

**Leukemic Infiltrates. Leukemic Lymphomas.**—Wherever there is lymphatic tissue, a proliferation of either the lymphadenoid or myeloid forms may take place in leukemia, especially in the chronic lymphatic type. Peyer's patches enlarge considerably, become pale, and if they ulcerate, resemble typhoid ulcers. This picture is occasionally seen in acute leukemia which runs a malignant course, and the differential diagnosis from typhoid may present serious difficulties, clinically (comp. Veszpremi, Herxheimer, lit.). The tonsils, all the pharyngeal adenoid tissue, the thymus and mediastinal nodes are not spared, and may enlarge (mediastinal tumor; comp. there). Purulent destruction of the infiltrate may take place in the buccal cavity and it may be mistaken for

scarlet fever, diphtheria, etc. Heterotopic leukemic infiltrations which are called leukemic, diffuse or circumscribed lymphomas, may be observed in the liver, kidneys, heart muscle (comp. p. 83 under myocardium), serous membranes (pericardium, pleura, peritoneum, dura), more rarely in the skin (so-called lymphadeny, see under skin), the epididymis, the pia-arachnoid, the stomach, bowel, especially the cecum and appendix, the pancreas, even in the breast (see there). A diffuse infiltrating form has also been reported, occasionally involving whole organs, such as the kidneys, heart, mammae, testes, ovaries, uterus, bones, etc., (see Fabian). Aggressive tumor-like lymphomas appear more frequently in lymphatic leukemia, especially in the acute form; similarly, numerous nodules appear in the internal organs, (kidneys, spleen, liver), which may look like tumor metastases (comp. p. 203). Insofar as they appear in lymphatic leukemia, the opinion was formerly held that it was an infiltration of washed-in lymphocytes. According to our latest conception, however, they are either equivalent autochthonous overgrowths of preexisting adenoid tissue in situations where this tissue is usually but slightly in evidence, or the leukemic tissue-forming-noxa makes its chief attack on the undifferentiated mother cells of the blood-forming tissue and stimulates it to proliferation in one or the other direction (lymphadenoid or myeloid, see lit. by v. Domarus). For proliferations in myeloid leukemia, see p. 201.

A pronounced hemorrhagic diathesis often appears quite early, especially in the acute lymphatic form. Hemorrhages occur in the eyes, serous membranes, mucous membranes, skin, heart muscle, lungs, brain and its meninges; the hemorrhagic diathesis is far more unusual in chronic leukemia, and is seen only in its advanced stage. In most cases an increased formation of uric acid is found (see under kidneys).

An osteosclerosis affecting the whole skeleton is occasionally seen in leukemia (both forms) (lit. by Sternberg, Assmann, and Fabian). It is partly an accidental combination, and partly a later stage of an hyperplastic bone marrow process (Neumann-Heuck). Osteosclerosis appears also in pseudoleukemia, but very infrequently (see v. Baumgarten's case).

Charcot-Neumann crystals are found in the blood after death, (and also by splenic puncture in the living). They also appear in the bone marrow, spleen, lymph node pulp and liver, generally only after an increase of eosinophiles accompanying the myeloid form.

The etiology of leukemia, especially its typical, *i.e.*, chronic forms, is still obscure (see Naegeli, v. Domarus and others). Lowit's hemameba have not been found by others (Turk, Bloch). Ehrlich assumed there was a specific toxin concerned. Perhaps an infectious-toxic factor is responsible as some authors think (lit. by Sternberg), or presuppose

(Glanzmann v. Hansemann), with qualities similar to those producing myeloid organic changes in certain septic conditions (Naegeli, E. Meyer-Heineke); in the latter, however, the changes are confined within narrow limits (comp. Gans). Proescher reported finding spirochetes. Eug. Fraenkel and Much, Much and Hegler, Arndt and others found granular and Gram positive antiformin-fast bacilli in the lymphatic type (comp. in lymphogranulomatosis, p. 271). The relation of leukemia to status lymphaticus has been studied (see Herz, Barrenscheen). Traumata, especially of the spleen, as etiologic factors must be regarded sceptically (comp. v. Domerus), but the possibility of an exacerbation by trauma must be admitted (see Hirschfeld). For the experimental induction of leukemia in chickens, see Ellermann and Bang; in dogs and monkeys, see Ludke; also J. L. Burckhardt, v. Wiczkowski, Henschen. For cultural experiments from leukemic blood according to the Carrel method, see Awrorow.

According to Sternberg, an infection is the usual cause of acute leukemia, and there is only a difference in degree between a myeloid and a lymphatic reaction in ordinary acute infections (usually by strepto- or staphylococci) and real acute leukemias; the latter, instead of being a leukemia, is only a general infection with a leukemoid blood picture and corresponding condition of the hemopoietic apparatus. But, according to Naegeli, a reconsideration of this generalization is advisable, since there are cases with absolutely negative bacterial findings, not to speak of the possibility of a secondary infection (comp. Steffans). This question is by no means settled (see Herz, Paltauf, Beltz, Jagic a. Schiffner v. Domarus, lit.).

Banti, K. Ziegler and Ribbert, pleaded for the neoplastic nature of leukemia, and Banti, who at the same time believed in its infectious character, calls the two main forms systemic lymphadenoid and systemic myeloid sarcomatosis of lympho- and hemopoietic organs.

The author supports Veszpremi by believing that slight similarities in the histological picture do not justify such deductions, since the disease by no clinical or anatomical tests represents the cellular new growth which we require of a true tumor (see tumors of lymph nodes; see also the criticism of Pappenheim, Fabian-Naegeli, Schatiloff and others). Congenital leukemia is no longer recognized as such; the cases described with congenital universal hydrops, (Schridde), are only marked myeloid reactions with enormous erythropoiesis (erythroblastosis), caused by an etiologically unknown factor (toxins from nephritis of mother?) which injures the hemopoietic apparatus (comp. p. 240, under spleen). (Lit. of leukemia in appendix; p. 198).

Appendix.—Pseudoleukemia, in a narrow sense similar to aleukemia, aleukemic lymphadenosis, or aleukemic myelosis, is anatomically essen-

tially identical with leukemia, and like it, is a systemic disease of the lymphatic and myeloid tissue system. The difference is clinical, depending only on the absence of one symptom, *i.e.*, typical blood findings; the characteristic invasion of white cells into the blood is absent. In the lymphatic form, there is generalized enlargement of lymph nodes; in the myeloid form, which is very rare—the author saw such a case in a 62 year old man (see I Diss., Bornee)—the big splenic tumor predominates, (in this case, 1777 gms.), while the lymph nodes may not be involved (as in our case). See Sternberg, Diel and Levy. The hemoglobin content decreases with the increasing anemia. This disease is etiologically as obscure as chronic leukemia. Hypothetically it is considered an infection (lit. by Hirschfeld, Pinkus, Herz, v. Domarus, Lepehne, Diel and Levy). There are hematological transitions between aleukemia and leukemia (comp. Minkowsky, lit.), and we speak of leukemia with an aleukemic precondition (Troje, E. Meyer and Heineke and others); according to Naegeli, given time, the aleukemic myelosis always shows transitions to the typical myelogenous blood picture. This does not hold, however, in the case of the 62 year old man mentioned; he remained aleukemic; the leucocytes were only doubled in number; younger forms, especially myelocytes, were only slightly increased. There seems, indeed, to be only a quantitative difference between it and leukemia. Donecke thinks aleukemia in older individuals might be explained by a pathological reactive power on the part of the tissues, especially the bone marrow. Banti explains it as the infiltration of the vein walls and bulging of the endothelium inward; the lymphatic or myeloid tissue masses, penetrate the wall in true leukemia and reach the blood current, but not at all, or only slightly, in pseudoleukemia. Naegeli considers academic the separation of aleukemic lymphadenosis and myelosis from leukemia. Compare pseudoleukemia under spleen, under lymph nodes in which other forms of this symptom complex are discussed, and under skin where the only localizations may be nodular infiltrations as observed by the author in the lymphatic form, and as described by Hirschfeld.

### Impurities in the Blood

**Pigment, Air, Fat, Etc., in the Blood.** Pigments.—A black or brown pigment may appear in the blood in malaria (see p. 210) (melanemia). In icterus neonatorum and in acute atrophy of the liver, bilirubin crystals may be found (fig. VI, plate II appendix); in the icterus of adults, bile pigment in solution is present (cholemia) so that the foam of the blood becomes yellow. Brown discoloration is the result of methemoglobin (comp. p. 215). Coal pigment may reach the blood by the rupture of a lymph node (comp. p. 254), and pass into a vein or pulmonary artery.

Finally, most of the pigment granules are deposited in the spleen, liver or bone marrow.

Pneumonatemia results from air passing into gaping veins, especially the jugular, axillary, and the dural sinus, sometimes during operations; embolism in the left heart must be considered, (comp. Beneke, Brauer, lung puncture, Schlaepfer, lit. and especially Gundermann), especially in placenta praevia (Olshausen; opposed, Jlyin). Simmonds found gas embolism after the injection of oxygen into the tissues, Siebert, in artificial pneumothorax; Beneke saw air taken up by the intact alveolar capillaries of suckling babies as a consequence of excess intrapulmonary pressure; see Fuks. When air bubbles reach the right heart, they may pass to the lungs (air embolism) where even relatively large quantities are quickly absorbed by the blood; but if the amount is too large for absorption, the air emboli may displace sufficient blood to cause death by asphyxia (shrieks and spasms), as in ordinary air embolism (comp. Wolf). In other cases, the air travels further to the left heart, (to which it may find access also by a direct route, as after lung injuries), by way of the pulmonary veins, and thus into the greater circulation, especially the coronary and cerebral arteries. In the latter, the macroscopic air bubbles, especially in the basal vessels, produce miliary anemic foci of softening; they sometimes give clinical symptoms as do other emboli and thromboses; according to Brauer, they even cause sudden death (Wewer, lit.). Large masses entering quickly remain in the right ventricle which holds the air like a balloon, and compresses it without expressing it; the consequence is acute cardiac paralysis (Cohnheim). Others consider fatality from air embolism a combination of pulmonary and cardiac death. See experiments by Schumacher-Jehn, Kleinschmidt, Jehn-Naegeli, Gundermann. Large foamy air and blood mixtures may also cause death if they remain for some time in the right ventricle, as in a woman just delivered in whom uterine atony necessitated thorough packing of the uterus with tampons. According to Behm, even the use of a vaginal irrigation apparatus, especially the so-called balloon syringe used to produce abortions, may introduce a fatal air embolus from the uterus (see Heinze, lit.; Marmetschke, compare the case of vaginal hematoma described; see also Fink, lit.). We must take the fact into account that cadaveric decomposition produces gas bubbles in the blood. Care during autopsy!

Do not cut ribs, do not disarticulate sternoclavicular ligament since the subclavian veins may be cut and suck in air, especially during lifting of the sternum. Do not open the skull first, cut sternum across at level of II rib using the saw, then open right ventricle under water.

Fat in the Blood.—See under fat embolism in the lung. The destruction of fatty tissue, *e.g.*, after fractures involving the bone marrow, may

allow fluid fat droplets to enter the veins, and be carried to the right heart and thence to the lungs. Some of the fat passes through the lungs and becomes wedged in the capillaries of the brain, heart, kidneys, etc. In "indirect" fat embolism, the fat enters the blood by way of the lymph channels, even after mere bone concussions (Fritzsche, lit.).

Dissolved and saponified fat is present in the blood physiologically, especially during digestion. The fat content is increased, among other reasons, by chronic alcoholism, (Immermann), phosphorus poisoning (Puppe), poisoning with chlorine salts (Winogradow), in pregnant women and during the puerperium (Virchow); thus fat embolism may occur in these conditions. But the most marked lipemia occurs in some cases of diabetes; as much as 28% of fat has been found (lit. by B. Fischer, Paltauf, Marchand, Busse). The veins on the cardiac and cerebral surfaces and in the mesentery and omentum may appear as if injected with milk.

Substances in solution appear in the blood in many systemic diseases. We may mention those coming from exogenous sources, such as absorbed poisons (phosphorus, alkaloids, etc.), and those from endogenous sources such as uric acid in gout, or urinary constituents in uremia, glycogen—some in white blood cells, some free in the form of droplets—especially in diabetes and leukemia, glucose in diabetes (in small amounts, it is physiological like glycogen), and peptone, observed in leukemia. Ptomaines and toxic bacterial metabolic products or so-called toxins, (see under tetanus p. 213), are found in various infectious diseases.

### Parasites in the Blood

Their presence is of great general pathological and clinical interest, but will be discussed only briefly.

**Animal Parasites.**—Malaria, (see fig. 113). Discovered by Laveran (1881), and verified by Marchiafava, Celli, and others. Golgi traced their development within the host, *i.e.*, the human body; Ross (1887–1898), stimulated by Manson, investigated bird malaria in which the host of the parasite is the genus culex pipiens, and acquainted us with the development of the parasite in the intermediate host, the mosquito zanzares, and, according to Grassi, the genus anopheles claviger (see Doenitz, lit. Kossel, in reference to kinds of anophiles). These findings were verified by numerous investigators (lit. by Marchiafava and Bignami). For data on the malaria campaign in Italy, see Celli. The parasites are capable of ameboid movement (hemosporidia) and are found mostly in the blood of the victims during a chill, usually in the red blood cells (Kossel).

But there are also free (ectoglobular) parasites, among them the remarkable crescent forms, (Laveran's crescents), in estivo-autumnal, tertian, or pernicious malaria.

The developmental cycle of the parasites in human blood (see fig. 113), and in the mosquito body is as follows: in the beginning, a small non-pigmented body penetrates the red blood cell and enlarging, becomes an aschizont, a large body with pigment in the center. Then multiplication of the nucleus starts, and asexual development results, schizogonia, *i.e.*, a rosette-shaped division into segments, their number varying with the species; they are called merozoits, spores, or sporozoits. The merozoits are liberated by disintegration of the red cell and then enter fresh red blood corpuscles (fever). Schizogeny, asexual propagation, is repeated for some time in the blood of the patient. Bass and Jones not only succeeded in procuring schizogeny outside of the human body but had it continue ad libitum in pure cultures (comp. Olpp). But it is only within

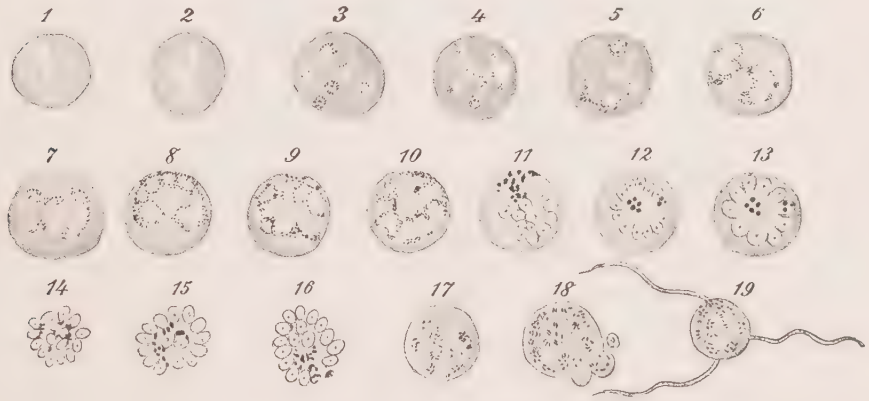



FIG. 113.—Tertian malaria. 1–10 Progressive development of the tertian parasite within red blood corpuscles. 11–13 Forms of division (schizogony) within red blood corpuscles. 14–16 Free sporulation. 17–19 Free pigmented degenerated forms (after Marchiafava and Bignami, Sulle febri malariche estivo-autumali, Roma, E. Loescher and C 1892 plate I).

the intestine of the blood-sucking anopheles which has become infected by feeding on blood of a human suffering from malaria that the ripening of the merozoits into sexual individuals takes place (male microgametocytes, and female macrogametes), thus insuring sexual propagation-sporogeny. From microgametocytes, microgametes develop, which are thread-like or flagella-like forms consisting chiefly of nuclear elements. These penetrate the macrogametes. The copula thus formed becomes the oocinete, a worm-like motile cell which bores into the intestinal wall of the mosquito. There it receives a delicate membrane, becoming an oocyst, *i.e.*, a sporont, which becomes rounded and develops numerous smaller cellular elements within, sporoblasts, which in their turn create numerous sporozoits, which are at first rounded, and later, when liberated from the body, are long and pointed with a long nucleus. One oocyte contains many (100 to 10000) sporozoits. The oocytes burst and the

sporozoits pour into the body cavity, but soon collect by active invasion in the salivary glands of the anopheles. When this mosquito bites, the sporozoits enter the wound with the saliva and thus the human victim is infected.

The microorganisms of malaria, according to Laveran, are of many forms, but of one species; Italian investigators, however, believe there are various species. They, and with them the majority of investigators differentiate: (*a*) plasmodium malariae (Laveran), in a narrow sense the cause of quartan fever; (*b*) plasmodium vivax (Grassi and Feletti), the cause of tertian spring malaria; (*c*) plasmodium immaculatum (Grassi and Feletti), the cause of tertian tropical fever (tropic, pernicious, estivo-autumnal fever).

In the blood, especially of the portal vein, are found black, reddish brown, or yellow and black, pigment granules, some free and some within leucocytes. Most of the pigment is formed by the parasites themselves from the material of the red blood cells, and lies within the body of the parasites. It is black (melanin) without the iron reaction, but a small portion is hemosiderin, which, subsequent to the destruction of erythrocytes by the plasmodia, enters the blood plasma (see Brown, Lohlein according to Seifarth, it is closely related to hematin). The pigment is deposited in various organs such as the spleen (comp. p. 235), the liver, etc. Iron may be excreted in the urine. Melanuria may occur. In malignant tertian malaria the organs contain large numbers of plasmodia in the state of schizogony. Partial or even complete obstruction of the cerebral capillaries explains the severe cerebral symptoms (coma, comatose malaria). (See among others, Durck in reference to changes in the central venous system. For malaria in general, see Celli, Ziemann, Schilling, Hartmann and Schilling, and others.)

Filaria Bancrofti or filaria sanguinis hominis (Lewis) were first seen by Lewis, especially at night (filaria nocturna), in the blood of patients suffering from hematuria and chyluria; he recognized them as the larvae or sexless embryos of a filaria (nematode). The length of the larva is 0.24 to 0.3 mm., the breadth 0.007 to 0.001 mm., (see fig. 114).

The fully developed, sexually mature animals (the female looks like a thin white thread and is 76–80 mm. long; the male 40 mm.), were seen first by Bancroft in 1876, then by Lewis in 1877. They dwell by preference in the lymph vessels of various parts of the body which become elephantic (scrotum, legs). Like trichinae, the young larvae enter the blood by way of the lymph stream, spread throughout the body, penetrate the blood vessels, and reach glandular organs such as the kidneys, lachrymal glands, etc. The larvae are found only in the peripheral blood during sleep. v. Linstow believes the capillaries are more dilated during sleep,

and permit ingress to the parasites, but Manson thinks a metabolic product formed during waking hours drives the larvae from the peripheral blood. Blood filaria may enter the intestines of mosquitoes of various kinds (culex ciliaris, tatigans, taeniatus; Manson). The bite of such infected insects transmits them to other hosts (Grassi and Noe, and others). Filariasis is found practically only in the tropics; it causes anemia, splenic tumor, fever, quite often lymphangiectatic filarious elephantiasis, especially of the scrotum and legs, swelling of lymph nodes, suddenly appearing chyluria, (the urine is milky from loose flocculates), chylous diarrhea and hematuria, (the urine is almost black), and inflammations of the kidneys, (these contain larvae, which may appear in the urine also), of the urinary tract,

FIG. 114.—Filaria nocturna in human blood, iron-hematoxylin stain. The outlines of red corpuscles not visible, but the nuclei of the cells which, with the two nematodes, were stained blue.

(see under bladder), of the peritoneum (chylous ascites), etc., (Winkel; Looss, lit.).

Other kinds of blood filaria are smaller and appear either in the daytime (F. loa, diurna) or both during the day and night (F. perstans). Firket found them in 55% of the negroes in Luttich, Congo, but found no disturbances in the general condition of the victims.

Distomum hematobium or Bilharzia hematobia, may occur in the blood of the portal region, the veins of the rectum and urinary bladder. From there, the parasites or their ova reach the feces and urine, (see bilharziosis, under intestinal parasites).

Of trypanosomes (protozoa of the class of flagellates), which are blood parasites but may also live in hemopoietic organs and tissue juices, only the trypanosoma gambiense (Dutton) will be discussed. It is the cause of sleeping sickness, with general lymphadenitis and encephalomeningitis combined (comp. R. Koch). It infests humans in tropical Africa, and is

transmitted by the bite of a fly (glossina palpalis) (fig. 115), which feeds chiefly on the blood of crocodiles. The tsetse fly can also transmit sleeping sickness from various big game animals (antilopes) to man (Kleine and Taute, Warrington Yorke and others, lit. E. Hofmann). The parasites are first found in the blood, later in the cerebrospinal fluid, and in the nervous system itself, and can be demonstrated in the cervical lymph nodes by puncture (Kuhn). They multiply in the blood by longitudinal division. See trypandas under skin.

In Chaga's disease (discovered by Chagas, 1909, in Brazil), which in its acute form is accompanied by fever, and swelling of lymph nodes, liver,

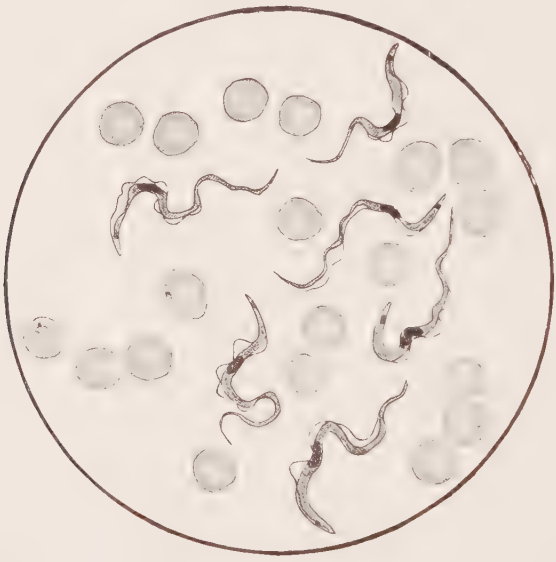


FIG. 115.—Trypanosoma gambiense in the blood of a patient with sleeping sickness. Long spindle-shaped body with cilia, undulating membrane laterally, large soma nucleus and smaller cilia nucleus, blepharoblast or centrosome, red blood corpuscles. Giemsa stain. Oil immersion.

and spleen, and in its chronic form, is frequently combined with goiter and cretinism (comp. Kraus and Rosenbusch, Novaes), a trypanosome (schizotrypanum cruci) is found in the blood. Their increase does not take place by longitudinal division, but by a form of schizogenesis in the tissues (fat cells, cross striated muscle fibres, heart muscle fibres) into which the young trypanosomes enter. After multiplying, the young may enter the blood. Transmission is through an insect (conorhinus C. megistus).

Of other trypanosome infections, see Kala-azar under spleen and oriental boil, or Leishmania tropica under skin. For trichinae in the blood, see under trichinosis in chapter "muscles." Staubli's method of demonstrating their presence consists of mixing and thinning the freshly

drawn blood, avoiding coagulation and contamination with an excess of 3% acetic acid. The parasites with the remaining leucocytic nuclei are sedimented by the centrifuge. This method is also useful for demonstrating various other parasites, both animal and vegetable.

**Vegetable Parasites, Especially Fission Fungi.** Anthrax Bacilli.—These remarkably plump, non-motile bacilli of 5 to 12 microns in length have been found repeatedly in the blood of humans with anthrax; they are most plentiful in the splenic blood which is dark and thin.

Sometimes it is possible to demonstrate anthrax only by injecting the blood into susceptible animals, such as guinea pigs or mice. Anthrax bacilli form spores in the cadaver, but not in living blood.

**Tubercle Bacilli.**—They are found in the blood of the cadaver, especially in the cardiac clots, also frequently in the living blood in acute miliary tuberculosis, more rarely in chronic phthisis, but at all times sparsely (lit. by Liebermeister).

Liebermeister found tubercle bacilli in the blood in 11 cases in 30, as proved by the injection of larger quantities of the blood into guinea pigs. Kennerknecht claims he found the organisms in 91% of tuberculous children. Kurashige found them constantly in phthisics by staining; but guinea pig inoculation is the only decisive method (see Kohler). Numerous investigations dealing with this matter are contradictory, but the consistent presence of bacilli cannot be entertained; they may possibly be found in miliary tuberculosis and in severe local tuberculosis (Randstrom, Rothacker, and Charon). Seidenberger and Seitz found them in latent tuberculosis. See also Bacmeister and Ruben, Rabinowitsch and lit. by E. Fischer.

The bacilli of glanders are very slender, almost as large as tubercle bacilli, and have been observed in the blood in acute glanders (see glanders, under nose). Glanders of the nose, skin, etc., is probably a localization of a hematogenous infection.

Bacilli can be demonstrated in the blood of almost every typhoid fever patient at some time or other (more details under typhoid, chapter intestines).

Among other bacteria found in the blood (bacteremia) we might mention:

Streptococci in septic, especially puerperal, diseases; staphylococci in pyemia, (see under osteomyelitis); pneumococci, (see pneumococcemia, p. 36); influenza bacilli, (see under bronchi); lepra bacilli, (see, for instance, Havelberg). Bacillus pestis has been found in the blood in cases with symptoms of septicemia (plague sepsis).

In tetanus, the bacilli, growing in manure and distributed in the earth by fertilizing the fields, were discovered by Nicolaier, 1884, in Flugge's

laboratory. Kitasato investigated the subject more carefully. Nissen and others demonstrated the presence of a toxin in the blood of infected human beings which in animals caused tetanus-like symptoms suggestive of strychnine poisoning, but of slower development. The severe symptoms of tetanus are the effects of the toxin. The bacilli can usually be found only at their point of entrance, from which the toxin spreads by way of the nerves to the motor ganglion cells of the spinal cord. The very resistant spores remain alive for a long time in street dust, or on infected wood splinters. See Reinhardt and Assim in reference to their effects on the internal organs. (Lit. of bacteriology of the blood by Jochmann and Cannon.)

**Spirochetae.**—It is still undecided whether they belong to the protozoa or to vegetable microorganisms (comp. Cf. B. Beil to sect. 1 vol. XII 1908).

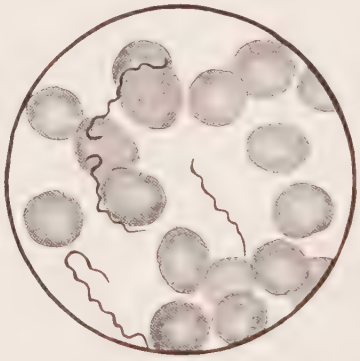


FIG. 116.—Spirillae (spirochaeta Duttoni) in the blood in African relapsing fever. Red blood corpuscles, four spirochaetae, Giemsa stain, oil immersion.

Spirochetae were first found by Obermeier, 1873, in the blood of patients suffering from European relapsing fever. According to many authors, they are found only during the fever. They show active movement, and are much more numerous in the blood than in recurrent African tick fever, the cause of which is the spirochaeta Duttoni. Bertarelli, by silver impregnation, demonstrated them in the enlarged spleen and liver; they were also found in the swollen intestinal follicles (lit. by Muhlens). The body louse (pediculus corporis) is its host, and transmits it, (see J. Koch); the spirochete Duttoni is transmitted by a tick, ormithodurus moubata. See Noguchi, Hata, for pure cultures of spirochaetae.

In Weil's disease (infectious icterus, icterohemorrhagic spirochaetosis) spirochaetae are in the blood in the first 10 days of the disease; they were discovered in 1915, (Inado and Ito, Hubener and Reiter, Uhlenhath and Fromme, see under icterus).

In yellow fever, which in the tropics is transmitted to man by a mosquito, stegomyia calopus, spirochaetae have lately been found in the blood

of patients (W. H. Hofmann); until recently a filtrable virus was suspected. (See Noguchi, J. Exp. Med., 1922 and '23.)

Numerous spirochaetae are often found in the blood in early syphilis, they are transmissible to animals, *e.g.*, the testes of adult rabbits (spirochaete pallida).

**Characteristic Blood Changes after Various Forms of Poisoning.** In carbon monoxide poisoning from coal gas, illuminating gas, (5–8 % CO) etc., the blood shows little tendency to coagulate and is bright cherry red. But the color is not always conclusive, *e.g.*, if a mixture of CO with much $CO_2$, as in coal gas, has been inhaled, the blood may be dark (Helfer). The CO combines with hemoglobin making carboxyhemoglobin in the cells which remain morphologically intact. In the spectrum, two bands appear at D and E almost identical with those of oxyhemoglobin, but those of the latter disappear after the addition of reducing substances (ammonium sulphide), leaving a thick band at D toward E; the bands of the former remain, even for months. The tannin test is also considered of practical value. Blood is diluted 3 times with water; by adding 1% solution of tannin, the mixture finally acquires a bluish red color (see J. Muller). For CO poisoning, see Wachholz; textbook of Lewin.

In poisoning by potassium chlorate (lit. by Winogradow), Marchand showed that the blood becomes brown, like sepia, from the presence of methemoglobin, a stable combination of oxygen with hemoglobin. In pure solution it shows an absorption band in the red (Dittrich) or orange (Todd, 1923). The erythrocytes disintegrate.

Various other substances also cause the formation of methemoglobin in the circulating blood, such as nitrobenzol, anilin phenylhydrazin, acetanilid, certain salts (iodides, nitrites), etc., (see Boehm). See Huber for bodies which appear in the erythrocytes.

**Lymph.**—Lymph consists of lymph plasma and lymph cells, practically all corresponding to small lymphocytes. Lymph is the light yellow fluid content of lymph vessels and serous cavities. "Lymph" is not a uniform conception (see Leon Asher, lit.), and must be differentiated from tissue fluid which is derived from the blood and is found in tissue clefts in the intercellular and interfibrous spaces (blood lymph, comp. p. 3). Blood lymph is also called nutrition exudate, because it gives up its oxygen and food material and takes up catabolic products of tissue when it becomes tissue juice; this is absorbed by the lymphatics, becomes more or less altered by the endothelium, and is then called lymph. A tissue overfilled with blood lymph and tissue juice can also be cleared by reabsorption into the blood vessels (comp. p. 4). When the metabolism of an organ is increased, more lymph pours from its lymphatics (Asher). Lymph

coagulates with more difficulty than blood; in the cadaver normal lymph is a clear and fluid admixture received from areas of varying constitution. Thus, for example, part of the food is contained in the chyle vessels and their lymph looks like milk. It picks up cells during its passage through lymph nodes.

The composition of lymph changes under pathological conditions; decomposition products of the exudate are contained in the lymph coming from the lungs when a fibrinous pneumonia is resolved. It becomes turbid and milky. Lymph having its origin in inflammatory tissue always shows more cellular elements, and may contain desquamated endothelium and fibrin flocculi. After bone concussions, fat from the marrow may enter the lymph indirectly (see p. 208).

In acute cerebral disintegration subsequent to anemic necrosis, hemorrhage, etc., the debris is mixed with the lymph and appears in the perivascular lymph sheaths (illustr. under brain). Large numbers of red blood cells may be found in the lymph after hemorrhage.

Pigment, too, which has entered the body from without, such as coal dust, pigments used for tattooing, etc., may reach the lymph; or it may be contaminated by bacteria or tumor cells.

If the circulation is permanently checked, the lymph eventually thickens to a white detritus.

## BLOOD MAKING ORGANS

### SPLEEN

**Anatomy** (Fig. 117).—The spleen is surrounded by a delicate fibrous capsule covered by a single layer of endothelial (or epithelial) cells continuous with the peritoneal cellular lining. This capsule has bundles of smooth muscle fibres in its inner layers. From it, the fibrous trabeculae, rich in elastic fibres (fig. I-b), with which a few smooth muscle fibres are mixed, extend into the depths of the organ. They form a coarse network, act as a scaffolding, and are paths for the larger vessels.

The arterial and venous trunks enter and leave at the hilum.

The large meshes formed by the trabeculae are filled with a fine reticulum of cells (fig. I-e1), and numerous branching veins (fig. I-e2.) This is the pulp with its capillaries and cavernous veins, inappropriately called splenic sinuses, and also called "capillary splenic veins" (see Schaffer).

In this fine network are gray nodules and branching strands, the follicles, (Malpighian corpuscles),(fig. I-c), scattered at regular intervals.

The follicles consist of adenoid tissue, (fig. 125 under lymph nodes), and are so connected with the ramifications of the splenic artery that they

surround the vessel (fig. I-d) like a coat. This coat shows spindle shaped or globular swellings here and there, and is supplied by a network of capillaries. The follicular meshes contain lymphocytes. On section, the follicles appear rounded, cylindrical, or branched, according to the the section.

The pulp consists of a network of fibres and dividing walls composed of prolongations and bodies of large, flat endothelial cells, (reticulum cells), each containing an oval nucleus. In the meshes are larger oval or round cells containing one or more round to oval vesicular nuclei, the true

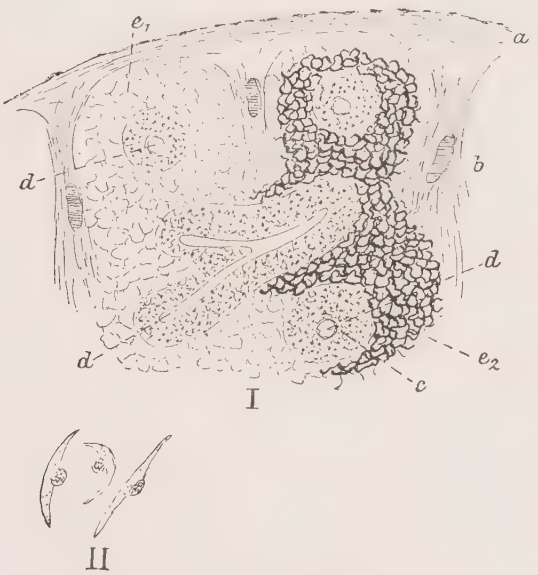



FIG. 117.—I. Spleen diagramatic (partly after Klein); a, fibrous capsule covered with endothelium, sending trabeculae or septa (b) into the organ. In the septa run the large vessels, between the trabeculae lies a coarse meshwork filled with pulp tissue and containing cavernous veins. These latter are drawn in $e_2$ into the pulp, not in $e_1$. c, Follicular tissue with finest reticulum, containing cells; d, central artery in the follicular tissue. II. Isolated endothelial cells of the cavernous capillary splenic veins (pulp smear) (medium magn.).

spleen or pulp cells (splenocytes), about which there are doubts as to whether they are lymphocytic (Naegeli and others) or myeloid (Paremusoff), or are an especial cell because of their phagocytic properties which are not shared by lymphoid cells in general.

The pulp also contains occasional lymphocytes, leucocytes and erythrocytes; debris of the latter may be held in macrophages (phagocytic pulp cells); blood corpuscle-containing cells are called pigment granule cells. Occasionally some free yellow or brown pigment is found (see Brotz in ref. to plasma cells). These cells do not completely fill the meshes. In the pulp which is arranged in strands, lie thin-walled, wide vessel net-

works (e2), the capillary cavernous splenic veins. They have an especial kind of long slender endothelial cell with sharply projecting plump oval nucleus. The cells are markedly phagocytic under certain conditions. All the meshes of pulp and follicles are intercommunicating.

The blood circulation in the spleen is as follows: The splenic artery enters through the larger trabeculae, then quickly splits into small branches without forming lateral anastomoses (end arteries); they then pass through the follicles, *i.e.*, they receive a covering of lymphoid tissue (see above), to which they give up small, many-branched twigs; after leaving the adenoid tissue they break up finally in brush-like continuations, (splenic pencilar arteries), entering the pulp as capillaries. Immediately before the capillaries, the arterioles become thicker and narrower for a short distance from the addition of husk-like fibrous longitudinal layers, (husk arteries), which probably afford protection to the delicate venous capillaries of the pulp against sudden excessive flooding. These husk arteries early undergo arteriosclerotic changes (see p. 114). The blood then enters the cavernous veins, and from there passes into venous trunks which traverse the trabeculae toward the hilum, uniting to form the splenic vein. The splenic circulation is by no means perfectly understood. The intermediary circulation especially, is doubtful. According to one theory, the blood, after passing from the follicles into the pulp capillaries and cavernous veins, pours freely through gaps in the latter into the meshes of the pulp, but Billroth, v. Ebner, Thoma and others, on the basis of injections, claim that the vascular system is closed, *i.e.*, lined with endothelium; the vessels, nevertheless, are highly permeable to fluids and to diapedesis of cells, especially the reticular perforated wall of the cavernous veins; thus free communication is permitted between blood and pulp (comp. Janosik, Helly, and especially Mollier). [See Robinson, W. L.; Am. J. Path., 2, 341, 1926, for admirable exposition of the vascular mechanism of the spleen.—*Translator.*]

Lymph vessels form capillary networks in the capsule communicating with the lymph vessel networks of the trabeculae, and these in turn join with the networks of the adventitia of the arterial trunks (Klein). Nerves, principally non-medullated, enter at the hilum, are abundant in the trabeculae, and supply the musculature.

The weight of the spleen in the new born is about 9 gms., (other figures by Herrmann). In adults, according to Krause, it is 150 to 250 gms. with considerable fluctuation, but Krause's values are too high for normal spleens; those above 120 gms. are probably not normal. The lower limit is about 90 gms.

Measurements: length, breadth, thickness about 12, 7 to 8, 3 to 4 cm. in adults.

Macroscopically, the following parts are recognized. Capsule, trabeculae (whitish), pulpa (red or brown red) and follicles (grayish white). (See also Sobotta for anatomy of the spleen.)

Functions of the Spleen. In the fetus it is myeloid; erythrocytes and myelocytes are manufactured in the pulp which is relatively large in amount. It may still show erythropoiesis physiologically in young individuals, and later under pathological conditions (see under myeloid metaplasia, p. 201). The spleen gives lymphocytes to the blood as they are produced in the follicles, (lymphocytopoiesis); in the absence of lymph channels they reach the blood directly. Some assume that the pulp also forms leucocytes (see Schaffer). One of its most important functions is phagocytosis, which is practiced on many substances such as blood cells or foreign bodies, (see p. 222), detritus of blood, used-up platelets, (Bernhardt), decomposition products of leucocytes and especially erythrocytes (Frey). Ehrlich characterized the spleen as a spodogenous organ. Pulp cells, reticulum cells and endothelium of the cavernous veins, all participate in erythrocytophagia. Physiologically, only broken down erythrocytes are seized, but under pathological conditions, whole erythrocytes are taken up by endothelium and pulp cells, as in infections, especially typhoid fever, and in grave anemias (blood corpuscle- and pigment-containing cells).

The spleen plays an important regulatory part in iron metabolism (Asher, M. B. Schmidt). Broken down erythrocytes are phagocytosed in the spleen and the iron is retained (iron-containing pigment granules), together with the iron derived from tissue disintegration elsewhere, while the iron consumed with the food is stored in the liver. A further function of the spleen consists in utilizing the iron in building hemoglobin (Bayer) and also in preparing for bilirubin production in the liver. As Bayer has shown, in Banti's disease, *i.e.*, pathological conditions, this power of retention may be preserved, but the capacity to elaborate the iron is lost.

Splenectomized animals eliminate more iron in the feces (comp. Chevallier and references by Schmincke).

The reticulo-endothelial metabolic apparatus. After splenectomy, endothelial cells of the liver, lymph nodes and bone marrow vicariously undertake the phagocytic functions of the spleen (Pearce and Austin), and especially the Kupffer's cells of the liver store iron, collargol, etc., (M. B. Schmidt, splenic tissue of liver). The manifest functional relationship of reticulum cells (endothelium), endothelium of the lymph sinuses, splenic veins, liver, bone marrow and adrenal capillaries, as already mentioned on p. 198, together with certain free cells equipped with phagocytic properties, *i.e.*, macrophages, histiocytic blood cells, histiocytes (Aschoff-Kioyono), have led to the conception of a reticulo-endothelial

metabolic apparatus (see also Kaznelson). Its importance in addition to phagocytosis, etc., probably consists in being a significant connecting link between the functions of the spleen and liver (hemoglobin metabolism and iron storage, comp. McNee, Lepehne, lit.) and probably also of the other organs mentioned (Landau). Lubarsch considers the apparatus a part of the macrophage system, *i.e.*, a system of cells which take up particulate matter which is broken down, or precipitated from the fluids.

For the relation of the spleen to fat absorption, see Schmincke (lit.) and Siegmund. There is said to be an increase of blood fat after splenectomy in animals, and the spleen may be an intermediary organ in cholesterin metabolism (Landau). In spite of all this, the spleen is an organ which can be dispensed with by most people, but some individuals react after its excision with severe disturbances, among them polyglobulia, which suggests the removal of a possible, thus far undetected, hemolysin in the spleen, and also, more probably, pre-supposes an increased bone marrow activity, because the spleen may have an inhibitory influence on bone marrow function through hormones (Frank). See p. 188, and Naegeli (lit.) as to other alterations of the blood picture observed after splenectomy, such as lymphocytosis, eosinophilia, increase of monocytes, appearance of Jolly-bodies. In rabbits the blood picture does not change (Port).

Splenectomized animals are said to be more resistant to blood poisons and also to infections. More in reference to hepato-splenic diseases by Eppinger, Ranzi, and in the section on icterus hemolyticus.

### Congenital Anomalies

**Congenital and Acquired Displacements.**—Absence of the spleen is very rare, and occurs in monsters, especially anencephales, with extensive defects of other abdominal organs, as well as in well-formed individuals, who indeed may live to a very old age (Sternberg). Accessory spleens, one or several, are occasionally found as small rounded bodies near the spleen in the gastro-splenic ligament in which the splenic artery is situated, or more distant (Schilling, lit.), as in the tail of the pancreas, rarely in the head, where the author saw accessory spleens the size of a cherry. Sneath described an accessory spleen in the scrotum which suggested a third testis and which was connected with the main organ by a pedicle. In an unusual case of H. Albrecht, 400 accessory spleens were scattered over the whole peritoneum; in such cases, Beneke thinks of traumatogenous fragments, later undergoing regenerative enlargement. See also the case of Winterer, and Kreuter's experiments with monkeys. On the other hand, 5 years after splenectomy done for crushing trauma, injury by gunshot, Faltin and Kuttner saw numerous small spleens on the peritoneum, (Kuttner about 1000), which were interpreted as compensatory growths (see also

Stubenrauch). Accessory spleens are constructed like the spleen and participate in its diseases. But others are transitions to lymph nodes, or are practically lymph nodes.

Lobulations of the spleen, shallow or deep, often several indentations of its edge, may be congenital and must not be mistaken for the scars of infarction. Accessory spleens may also be present and occasional developmental faults in other organs. Under such conditions, lobulation of the spleen as a minor organic fault is merely one indication of an entire constitution faulty and defective.

**Displacements.**—Displacement, ectopy, is spoken of when the spleen has been displaced from the abdominal cavity into the pleural cavity or into the sac of an umbilical hernia. The first occurs in congenital diaphragmatic rupture.

Displacements within the closed abdominal cavity are of more importance. These occur (*a*) upwards, *i.e.*, up and backwards in ascites, pregnancy, abdominal tumors, etc.; (*b*) inward and anterior, which is rare but occurs occasionally, *e.g.*, with left hydronephrosis (see picture there); (*c*) downward, these are most frequent and important and occur with otherwise normal spleens, *e.g.*, in women from tight lacing, but particularly in pathologically heavy spleens, the so-called splenic tumors in which the weight pulls the spleen downward, thus stretching the ligaments (gastro-splenic and phrenico-splenic) and with them the splenic artery. If the ligaments have lost their previous normal tonus from pregnancies, ascites, abdominal tumors, etc., the spleen may slip from its normal position even if not heavier than usual. Low position of the diaphragm and tight lacing may force it downwards.

It may remain fixed in its altered position or may remain more or less mobile (floating spleen). The hilum lies upwards, with the convexity downwards. The artery may become twisted and cause atrophy. The degrees of displacement vary. The direction is towards the left downward, or towards the sacrum diagonally across the abdomen to the right downward (lit. in ref. to floating spleen in gynecology by Montuoro).

In a case in Breslau, (G. Klein), the spleen, 17 cm. long, lay in the small pelvis between the bladder and the retroflexed uterus which was forced against the sacrum; it had been lifted up by means of a pessary as a retroflexed uterus.

### The Spleen as Receiving Station of Substances Contained in the Blood

Ponfick and others have shown in animals that pigments introduced into the blood are deposited in the splenic pulp.

Leucocytes act as carriers. Later experiments with carmine showed deposit in pulp cells, sinus endothelium and free macrophages lying in the

sinuses and derived from its endothelium (Steudemann, lit.). It was proved in man that inhaled coal pigment (anthracosis) is carried through the bronchial nodes into the blood and thence to the spleen (Soyka), for, as Weigert has shown, nodes discolored by coal pigment may soften and rupture into the vessels, permitting the pigment to enter the blood. Arnold pointed out the possibility of direct penetration of pigment into the blood through thin vessel walls, especially in emphysematous lungs.

Anthracotic pigment selects especially the adventitial sheaths of arteries, and surrounds the follicles as well as enters them. It often lies in large spindle shaped or branching cells (endothelial). The endothelium of splenic veins and pulp cells also contains pigment. Anthracosis of the spleen is frequent in old people and in those who handle quantities of coal. In marked anthracosis, especially if rupture into a blood vessel has occurred, black dots and striae, up to the size of a pinhead, appear on the section surface. This is more easily seen in colorless alcohol preparations than in the fresh bloody organ.

In malaria, black granular pigment from the blood is deposited in abundance in the reticulo-endothelium of the spleen (and liver) (p. 235).

In diseases in which large numbers of red blood cells are destroyed (see under blood, p. 186), a large part of the pigment thus liberated is taken up by the spleen, and after burns, cells are found containing blood corpuscles (Askanazy, Perewalowa). The spleen swells, becomes rust colored, reddish brown, lava or chocolate colored (methemoglobinoemia, see p. 215), due to the deposit of pigment masses, some in the reticulum cells along trabeculae, pulp cells, connective tissue cells of the trabeculae and some simply imbibed. The resultant swelling of the spleen is called spodogenous (Ponfick).

In icterus neonatorum, bilirubin crystals are found in the spleen; in the icterus of adults, diffuse pigmentation occurs. The spleen is large and soft.

In many infections such as typhoid fever, anthrax, etc., the organisms are carried by the blood to the spleen where they cause inflammation. Saprophytic bacteria, and likewise pathogenic organisms with decreased virulence, (comp. J. Koch), introduced into the blood of animals are, as Wyssokowitsch has shown, eliminated in a few hours (in Koch's experiments in $\frac{1}{2}$ hour) and deposited in the spleen as well as in the stellate cells of the liver and in the bone marrow. In the spleen, they are partly free, and partly in pulp cells, blood vessels, and follicles where they are soon destroyed. But it is interesting to know that splenectomized animals resist infection not only as well as normal animals, but perhaps even better (see Hirschfeld and p. 220).

Decomposition products originating in inflammation are also deposited in the spleen. Thus Gerhardt assumes that in pneumonia the increasing

enlargement of the spleen, even after the crisis, is a spodogenous splenic swelling, *i.e.*, caused by the deposit of decomposition products from the liquefied exudate of the alveoli, which calls forth an increase of the pulp cells to reduce the debris.

It is also interesting that the part played by the spleen as a place for deposits is contradicted in a way by the behaviour of tumor metastases (p. 247).

### Circulatory Disturbances

The blood content, color, and volume of the spleen vary within broad limits; thus it becomes larger and more vascular during digestion.

**Anemia.**—In acute anemia, the volume is diminished, the capsule is wrinkled, the consistency increased, the color is pale grayish red, the follicles are indistinct while the trabeculae stand out relatively sharply. In chronic anemia, the spleen becomes small, tough and pale. For enlargement of the spleen in certain chronic anemias, see under blood, pp. 192 and 193.

**Hyperemia.**—Active hyperemia is, as stated, physiological during digestion. We see it in more marked degree as the first stage of the acute inflammatory splenic tumor of infectious diseases. Every enlargement of the spleen is called "splenic tumor;" more pronounced degrees of chronic enlargement are called "splenomegaly." See under inflammation of spleen, p. 230.

Passive or Obstructive Hyperemia.—Due to the numerous veins of the pulp, the position of the spleen in the vascular system (the splenic vein empties into the portal vein) and the absence of almost any anastomoses (only the smallest veins lead from the splenic capsule into the azygos vein), congestion is extremely frequent. Obstruction to the venous outflow may be of central origin, *i.e.*, from the heart, (valvular lesions especially of the mitral valve), or from the lungs (emphysema, interstitial pneumonia, adhesive pleuritis). The obstruction works backward in the hepatic-portal-splenic systems.

Congestion starting from the portal vein occurs in cirrhosis of the liver, syphilitic hepatitis, (see there), thrombosis of the portal vein which may continue to the splenic vein, tumors of the liver, etc. Thrombophlebitis of the splenic vein may be an extension of a pyelophlebitis which in turn may be an extension through the mesenteric veins from appendicitis; the spleen is soft and pulpy. The author saw one with conspicuous trabeculae and follicles, and dark red section surface, weighing 650 gms. In this specimen were combined obstruction and inflammatory hyperplasia. Congestion due to compression, or to an autochthonous thrombosis of the splenic vein is plainly seen in tumors, especially of the pancreas. Cyanosis

of the spleen is seen most frequently in cardiac and pulmonary diseases, and is most pronounced if the circulatory obstruction is in the portal vein. At first, the veins are distended, but if the engorgement is older, the walls and pulp reticulum undergo fibrosis, the trabeculae and the capsule thicken (cyanotic induration). The spleen enlarges, chiefly in thickness, becomes plump and the capsule is stretched, opaque and hard. The consistency is increased, and with longer duration, is actually hard. The section surface is smooth, at the beginning dark red, later bluish red to black blue with white striae and nodules corresponding to the thickened trabeculae.

In time, the hyperplastic connective tissue contracts causing atrophy of the parenchyma, and diminution in size, (cyanotic atrophy). The enlargement of the spleen in cirrhosis of the liver, especially in the hypertrophic form, differs from that due to obstruction from central causes. At first, as a rule, the increase in size is quite marked; it is only rarely that it does not enlarge at all, (weight 600 gms., even 1000 gms., exceptionally more). In ordinary cirrhosis of the liver the author saw a spleen weighing 1530 gms. while the liver weighed 1420 gms. The consistency is not so hard as in obstruction; the capsule may be stretched tightly; perisplenitis may be present. On section, the pulp appears moderately soft, slightly darker red in color than normal, or indeed lighter red. Abundant round cells showing fatty degeneration and much pigment deposits are to be found. The enlargement is due mostly to hyperplasia of the parenchyma, (pulp hyperplasia), with moderate thickening of the pulp reticulum (Oestreich) as contrasted with congestion. Schridde mentions the remarkable width of the sinus veins in this condition, which the author can verify and would emphasize especially as a means of differentiation from Banti's spleen (see below). There is a temptation to suppose that this enlargement as well as that accompanying the hypertrophic type of cirrhosis of the liver is due to the same stimulus which induces the cirrhosis (see, for instance, Egidi). But Hartwich considers splenomegaly the product of a compensatory hyperplasia in failure of liver function.

The splenic tumors caused by various other impediments in the portal circulation or in the course of the splenic vein itself, are also usually larger and softer than the congestion spleen of central causation. Congestive induration does not develop in these cases, since collateral channels permit relief.

Banti first described the symptom complex which bears his name, *i.e.*, splenomegaly with anemia, and finally, cirrhosis of the liver. The disease is a primary splenomegaly with progressive development of sclerosing connective tissue (fibroadeny) which leads to a not very pronounced anemia, but one somewhat like a severe chlorosis with a cor-

respondingly altered color index (see Isaac lit.), and a leucopenia. This anemia is due not to increased blood destruction, but to decreased blood formation and may be of many years duration; during an intermediate stage lasting 12 to 18 months, the liver becomes enlarged and a slight general icterus follows shrinking of the liver. Then there are ascites and all the symptoms of Laennec's cirrhosis. In this third stage, true icterus (see Quadri) and the hemorrhagic diatheses are absent. The spleen remains enlarged, and death occurs in one year. The splenic enlargement, (rarely less than 1000 gms.), is much more pronounced than in ordinary cirrhosis of the liver, and remains constant, as a rule, after attaining a certain size. Banti thinks of noxae, etiologically undefined, perhaps toxic (see also Umber), or infectious (see Luce), which enter the spleen from the blood; from here this noxa, now more potent, reenters the blood, disturbs the hemopoietic factors, causes anemia and is carried permanently into the liver. In the spleen, it causes a fibrous change beginning around the arteries (fibroadeny) in the follicles which usually are small. According to Banti, thickening of the reticulum fibres takes place without cell reaction, but others, as Chiari, believe in fibroblast formation. The injury also causes fibroadeny of the pulp with narrowing of the cavernous veins, destruction of pulp cells and a sclerotic phlebitis which extends to the portal vein. Blood pigment is never found in the pulp. Finally there is added a more or less marked hyperplasia of the connective tissue of the liver which leads to cirrhosis. The experiences of later years, however, have shown that not all cases develop cirrhosis of the liver. Most remarkable indeed are the permanent cures after splenectomy (see Armstrong, lit.). If the picture drawn by Banti is carefully considered, Banti's disease represents a well characterized symptom complex (see Port, Chiari). But the question of whether it is a separate or distinct disease may be answered partly affirmatively and partly negatively. Banti himself emphasizes the negative etiology, and this factor must be kept in mind. Syphilis (Chiari, lit., Marchand, see also under esophageal varices, observations of the author) malaria, tuberculosis, etc., must be differentiated. Luetic cases are very different from Banti's disease in reference to liver changes. Naegeli, on the other hand, claims observations in which a luetic etiology produced conditions in all stages similar to Banti's disease. The same has been said of (alcoholic) cirrhosis of the liver with a so-called precirrhotic splenic tumor. But the spleen of Banti's disease is histologically different from that of cirrhosis of the liver (see p. 224). It has been suggested that we add to the designation, Banti's disease, or splenomegaly with cirrhosis of the liver, the etiological diagnosis—lues, malaria, etc.—(Neuberg, Steiger), but it is incorrect to do so, inasmuch as at present when the etiology is demonstrable, the case automatically

ceases to be Banti's disease. Besides this, Banti's disease does not begin when splenomegaly and cirrhosis of the liver are present, but begins with an anemia, lasting perhaps for years, with splenic tumor and without cirrhosis of the liver. Banti, himself, in 1882, spoke only of splenic anemia, meaning an anemia caused by splenomegaly. It was only later that the cirrhosis of the liver was given an important place in the symptom complex, but since it is secondary, it really does not deserve such notice. The early stages, anemia and splenic tumor without cirrhosis of the liver, are by far the most important (see Isaac, lit.). Naunyn indeed proposed calling only such cases Banti's disease which show splenic tumor with anemia and no cirrhosis of the liver,—*i.e.*, cases of so-called splenic anemia. But splenic anemia itself is only a vague symptom complex, and splenic tumor and anemia are a frequent combination with varying characteristics; for this reason the conception, "splenic anemia," has been, or should be discarded (see Sternberg, Naegeli and others; see p. 193). The author observed two cases showing clinically the typical picture of Banti's disease, and microscopically the most pronounced fibroadeny in the spleen (compared with the original preparations of Banti); in one case there was no cirrhosis of the liver, while in the other case it was only just beginning. Fibroadeny of the spleen is not a specific process, as Banti himself emphasizes, because it may accompany a primary splenic or portal phlebitis, (see Gruber). Nevertheless it is not found to the same extent in the numerous secondary anemias combined with splenomegaly. The success of splenectomy proves also that the spleen is the source of these changes, and it is easy to think of elimination of a splenogenous noxa which checks hemopoietic activities in the bone marrow (Turk) (lit. in appendix).

**Translator's Remarks.**— It is useful surgically to distinguish between enlarged spleens, secondarily and primarily produced. Splenectomy in the former offers little encouragement; in the latter it may be curative, *e.g.*, in Banti's disease in a certain stage. The criteria on which the decision may be made rest on clinical grounds and on the pathologic anatomy as revealed at operation. The latter may be gathered from the text above; *cf.* also under cirrhosis of the liver.

### Embolism of the Splenic Artery

The splenic artery, very wide at its beginning, soon branches like a tree and resolves into end arteries; it is especially liable to arrest emboli circulating in the blood. Most emboli come from valvular lesions of the left heart, and the consequences depend on the nature of the embolus, whether benign or infectious, and on the size of the branch occluded.

**Simple (Non-infectious) Embolism.**—If the trunk of the splenic artery is completely occluded, the whole organ dies, changing into a brown, later yellow or grayish yellow mass, which at first is pultaceous and later dry; finally it becomes a caseous mass surrounded by a connective tissue capsule. It often undergoes calcification. When a branch of the splenic artery is occluded, the resulting infarct is anemic or hemorrhagic, a white wedge, or anemic sequestrum, or a red wedge.

FIG. 118.—Infarctions of the spleen. From a patient 24 years old. The thrombus of the vessel is seen in the center of the illustration. The upper end of the spleen shows red infarction. The wedge-shaped areas, lighter in color, are older infarctions which have been bleached. L. H. ×16.

In anemic infarction, the area supplied by the occluded branch simply perishes and undergoes anemic necrosis. The dying tissue loses its normal markings, changes its color, becomes in turn brown, orange yellow, sulphur yellow, clay colored, whitish yellow to white as the pigment disappears (M. B. Schmidt). It swells at first, bulging out the surface, but soon alters its consistency. Plasma entering from the surrounding capillaries

and the dying cells complete the coagulation necrosis (Weigert). Then the necrotic wedge is more voluminous and stiffer (fibrin wedge). From loss of water, it dries, and in about 14 days resembles the dry caseation of tuberculous lymph nodes. Microscopically, the follicles in this dead hyalin mass remain recognizable the longest; the cells lose their nuclei, break up in clumps and finally everything becomes homogeneous. In the vicinity of the infarct, a wall of fat-laden, glycogen-burdened leucocytes collects (yellowish zone), which also penetrate the edges of the wedge (more details by Ricker, Griesser, Dietrich). More rarely, this non-infectious, dead mass softens into a cavity, occasionally cystic with puriform (not pus!) yellow pultaceous contents.

In red infarction, the dead tissue is filled by blood from collateral channels; it becomes black red, and eventually dies. The infarct passes through other color changes, during which bundles of hematoidin crystals may appear microscopically; it becomes brown, flesh colored, grayish yellow, pale gray, clay colored and shrunken. Around the red or brown infarcts is a yellow angular border (yellowish zone, see above). When a red infarct is completely decolorized, it resembles an anemic infarct. Sometimes the collaterals discolor only the peripheral parts of the dead area so that a light colored necrotic wedge is surrounded by a dark red border.

Corresponding to the ramification of the arteries (end arteries) the shape of the infarct is approximately like a wedge or pyramid. The apex points toward the hilum and the base is underneath the capsule where it is sharply demarkated by a dark blue, brownish red, or light yellow bulging (hemorrhagic or anemic infarct). It may be palpated as a more resistant nodule especially on the sharp edge of the spleen, or may be discovered only after sectioning. If numerous and large, a considerable general splenic enlargement results.

Exceptionally, a border of splenic tissue at the base of the wedge is supplied by capsular vessels, and escapes necrosis.

Fibrin deposits on the peritoneal surface cause adhesions, and union with neighboring parts.

Further Fate of Infarcts.—If the dead tissue is absorbed, perhaps over a long time, the wedge shrinks and the original bulge disappears. Vascular granulation tissue containing many leucocytes proliferates from the periphery into this area changing it into a fibrous contracted scar (infarction scar) which may contain orange colored or rusty brown, mostly intracellular, granular pigment and caseous-calcified residue. Much pigment suggests a former hemorrhagic infarct. If numerous calloused contractions are present on the surface, the spleen becomes misshapen and lobulated. Covering the shrinking old infarcts and contracted scars is

the capsule, smooth or finely granular, or possibly fringy, or adherent to neighboring tissues, *e.g.*, the diaphragm, as a remains of the fibrous productive inflammations.

See Feitis in reference to peculiar spotted necroses (spotted spleen) due to arterial changes.

**Infectious Embolism.**—If the embolus is infected as from an ulcerative endocarditis, necrosis is also the first consequence of the mechanical obstruction, but very shortly, a circumscribed purulent process commences at the border by which the wedge is separated like the core of a furuncle. Pus gathers, the wedge liquefies and the pus-filled abscess cavity may still contain necrotic splenic tissue (Brockel) (pyosplenitis, suppurative splenitis). Ichorous changes occur when saprophytic bacteria, *e.g.*, from the intestine, become secondary invaders.

After destruction of the capsule, perforation into the abdominal cavity may follow and purulent or ichorous peritonitis result or perforation of the diaphragm or actual forcing of the wedge through it (see p. 233). The author saw this repeatedly in typhoid fever, although it must not be mistaken for purulent sequestrated typhoid necrotic foci (see p. 233); the embolic cause must be demonstrated. Others consider such abscesses or purulent splenic infarcts very rare in typhoid fever (Federmann), and Curschmann's monograph does not mention such a case. Griesinger saw wedge-shaped infarcts in 7%, C. E. A. Hoffmann in 3.6% (lit. Kuttner).

### Other Circulatory Disturbances

**Hemorrhages.**—In the acute infectious swellings, hemorrhages are frequent in the form of black red to brown dots with washed out centers. They are distinguished with difficulty from congestive hyperemia. Severe spontaneous hemorrhages may accompany typhoid fever, or result from traumatic rupture. Arterial branches have been eroded by a gastric ulcer.

Aneurysms of the splenic artery are saccular or varicose. Rupture may cause exsanguination into the abdomen (rare, see Binder). Pressure on the splenic vein has caused marked splenic swelling. Erosion aneurysms may develop from gastric ulcers (see there). Thrombosis of the splenic vein is seen in connection with splenic abscess or torsion in floating spleens; it rarely develops spontaneously; the spleen swells enormously. Thrombasis of intrasplenic branches produces less sharply demarkated venous infarcts. In simple thrombosis of the trunk, the parenchyma turns dark redish brown; in purulent thrombosis it liquefies into a green, foul smelling substance. For tumor thrombi, see p. 247. Splenic infarct may be followed by thrombosis of the splenic vein which may continue to the trunk of the portal vein (pyelothrombosis, details under liver).

Varices of the splenic vein, especially of its branches within the organ, are not rare. Frequently phleboliths to the size of peas are found. Exsanguination from a superficial varix is rare.

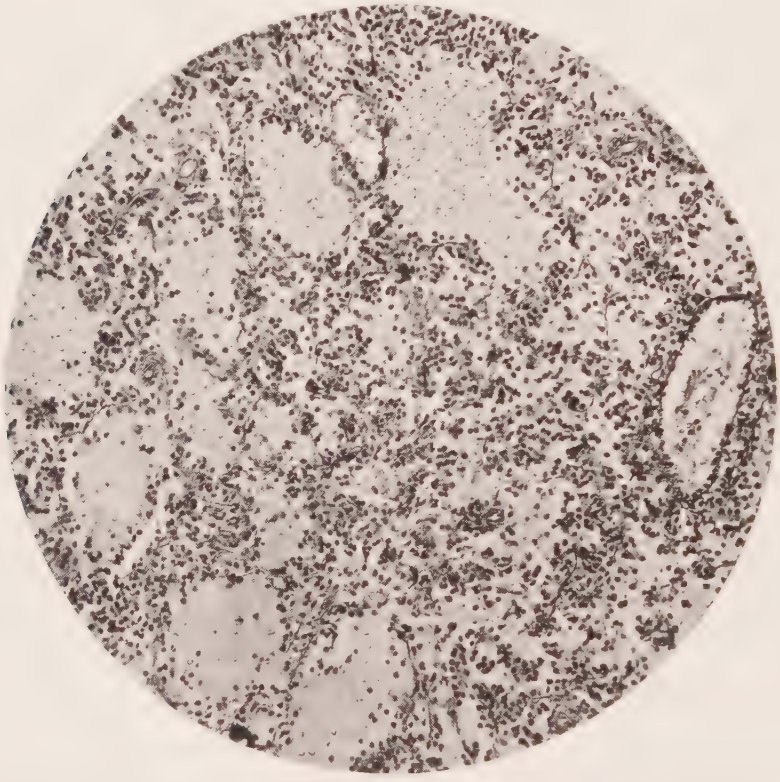


FIG. 119.—Marked prominence of the sinusoids in the spleen. Cardiac failure and passive congestion. × 120. L. H. #312.

### Inflammations of the Spleen

1. Acute inflammatory splenic tumor. Acute splenic hyperplasia. From the circulatory conditions in the pulp, especially the liberal communications between the perforated cavernous veins and the pulp, and the slowing of circulation in the pulp, agencies causing inflammation, especially bacteria and their metabolic products, have good opportunities to attack the spleen in its innermost parts. In truth, the organ is wonderfully sensitive to acute infectious diseases, especially if accompanied by fever, and in most of them we find participation by the spleen, either in the milder form of hyperemic swelling which may quickly come and go, or in the severe forms with varying degrees of enlargement accompanied by inflammation, or as inflammatory hyperplasia of the true splenic parenchyma (splenitis), especially of the pulp, less so the follicles.

For participation of the follicles, see under diphtheria; comp. also inflammatory softening and follicular abscesses, p. 234.

In hyperemic swelling the microscopic picture is essentially dilatation of the vessels, especially the veins and capillaries, and more marked filling of the pulp meshes with colored and colorless blood corpuscles. The swollen, hyperemic spleen may enlarge to two or three times its normal size, thus stretching the capsule. During life, the spleen feels hard; in the cadaver, it is soft. On the section surface, the dark vascular pulp bulges and covers trabeculae and follicles; by careless removal during autopsy the organ is easily crushed. Of importance in acute splenitis, *i.e.*, acute splenic hyperplasia, are the marked multiplication, enlargement and disintegration of cells which lie principally in the pulp strands, but partly also in the vessels (veins).

Some of these cells are lymphocytes as contained in the follicles, but the greater number are polynuclear leucocytes which have passed from the blood; in addition there are plasma cells, which, according to Huebschmann, appear constantly and often abundantly in many infectious diseases, especially in the periphery of the follicles, (see Marchand); others are proliferated pulp cells, rich in protoplasm. Many of the latter have several nuclei; others contain red blood cells or their pigmented fragments (erythrophagia), especially in typhoid and spotted fevers. Many cells disintegrate from fatty and granular changes, especially the swollen, characteristically crescent-shaped, venous endothelial cells. Red blood corpuscles are more numerous from the hyperemia. The causative organisms can often be demonstrated in the blood vessels, pulp and follicles, histologically if needful, and naturally, almost always, by culture.

In acute hyperplasia the spleen enlarges and becomes very soft, pultaceous and liquefying. It is called pulpous, since the cellular, grayish red pulp wells up as a soft material on the section surface and possibly covers trabeculae and follicles, and also since it contributes the essential part of the enlargement. Sometimes the pulp shows the dark spots of hemorrhage; in pyemia and septicemia, fatty degeneration is especially marked, and the friable, liquefying pulp appears pale grayish or reddish yellow. Many fragments of red blood corpuscles are seen, some in cells. The degree of acute splenic swelling varies with the kinds and amount of blood impurities.

In typhoid fever, a soft swelling is always present, and the weight may reach 500 to 600 gms., occasionally more; rarely, the weight is below normal; the author saw spleens of 140 to even 100 gms., the first in most severe, the latter in slight intestinal ulceration. The swelling is more moderate in pneumonia, increasing toward the crisis, while in anthrax

(with the organ very soft), acute miliary tuberculosis, recurrent fever, it varies from normal to considerably increased size. It is often remarkably slight in septicemia (toxemia) (150–200 gms.); in pyemia (bacteremia) it is often very considerable (up to 800 gms. and more); it is always soft and liquefying. In bubonic plague, it is not so soft, (Albrecht and Ghon), Crowell says: "firm," Durck: "soft," but it is always swollen, and the section surface is granular with a color similar to that of amyloid spleen. There are often subcapsular hemorrhages. In influenza, the swelling varies, but is usually slight; in cholera it is absent, as a rule. In uncomplicated scarlet fever it is slight, in septic cases marked (comp. Soxensen).

In diphtheria, the swelling is usually slight, the pulp is fairly firm but the follicles are somewhat enlarged and can be seen as gray or white nodules with cloudy centres. (In children the follicles are normally relatively larger and more plainly visible than in adults.) In the follicles are microscopic, large cell, pale foci (Bizzozero, Stilling), composed of cells which may be arranged in an irregular network and are supposed to be swollen endothelium, alongside of which are traces of reticulum (Ribbert). According to Councilman, Mallory and Pearce, the large, rounded, branching cells are proliferating endothelial cells of the reticulum which acquire phagocytic properties and take up and destroy lymphocytes. This change has been named focal necrosis and is called into existence by the toxic products of diphtheria. Councilman and Mallory have produced it experimentally.

Spontaneous rupture of the spleen with prolapsus of the soft tissues may occur in most insignificant happenings such as lifting, coughing, vomiting, etc., but is seen in rare cases in typhoid fever, abdominal miliary tuberculosis, leukemia, pseudoleukemia, recurrent fever, and still more rarely in amyloid spleen (Strada). Pain in the abdomen, increasing dullness in the splenic area, death with the aspects of internal exsanguination may all occur, or it may be repaired, if superficial, leaving a scar. For so-called spontaneous rupture, see under malaria, p. 235, and lit. by Melchior. See p. 246 for description of minute capsular ruptures and the formation of small "spleen hernias." See Borst for bullet wounds of the spleen.

Course. When an acute splenic tumor heals during convalescence from the causative disease, the capsule is too large and becomes wrinkled. The excess cells disintegrate by fatty degeneration and necrosis and are carried off. The color is dirty brown red from destruction of red blood cells, the pigment of which is mostly taken up by cells. Later, everything is perfectly readjusted, but in some cases a permanent atrophy leaves the spleen small and wilted, the trabeculae and capsule thickened, with adhesions to neighboring structures.

If the causative disease becomes chronic, the chronic splenic tumor is enlarged and indurated.

**Focal Purulent Splenitis. Abscess of Spleen.**—Purulent splenic infarcts have been mentioned on p. 229. Hematogenous metastatic abscesses are due, of course, to bacteria, but there is no demonstrable mechanical occlusion of a vessel.

Other splenic abscesses appear after trauma or by continuity from the vicinity (gastric ulcer, gastric carcinoma, pyelo-phlebitis, etc.). There must also be mentioned rare, etiologically obscure, hematogenous, so-called idiopathic, or better, cryptogenic abscesses the size of a pin's head to a fist, singly or, especially the metastatic, multiple, but rarely in large numbers.

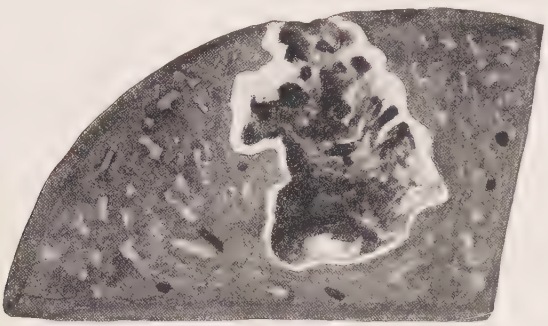


FIG. 120.—Splenic abscess; cross section of portion of organ of 59 year old woman; abscess perforated into the stomach.

Pus may undergo cheesy thickening and thus resemble anemic infarction, or tuberculosis; it may also calcify. Small abscesses may heal, leaving scar tissue.

Numerous confluent abscesses sometimes form a system of communicating cavities lined with a pyogenic membrane and filled with thick green pus. The enlarged spleen is completely excavated. This readily induces thrombosis of the splenic veins leading possibly to a portal phlebitis, pyelothrombosis and liver abscesses.

When the abscesses reach to the capsule, (quite common), the serosa shows perisplenitis, localized peritonitis, subphrenic abscess, (lit. by Piquant), or general peritonitis.

Sometimes a visible direct perforation is found through the capsule into the abdomen, or through the adjacent diaphragm into the pleural cavity. But more frequently the pus is localized in the vicinity of the spleen (parasplenitis), isolated by inflammatory adhesions from the rest of the peritoneal cavity (circumscribed peritonitis, subphrenic abscess). Secondarily, however, the pus may perforate the diaphragm into the pleural

cavity, lungs, stomach, intestine, or abdominal cavity. The author saw a perforated stomach which allowed gastric juice to excavate the spleen by peptic maceration. The cavity showed delicate transparent spider web-like branchings, remnants of the more resistant connective tissue structures.

**Rare Focal Diseases in Hyperplastic Spleens.**—(*a*) Inflammatory softening of the follicles was described by Ponfick in recurrent fever; the follicles were yellow and softened; the process, according to Nikiforoff, is a toxic necrosis. True follicular abscesses may develop in recurrent fever (Rabinowitsch, lit.).

(*b*) Pale wedge-shaped areas, the so-called necrotic wedges, which resemble embolic anemic infarcts, are sometimes seen in recurrent fever, in typhoid fever (4–6%), scarlet fever and typhus (Hlava), but more often in intermittent fever and leukemia. There is localized tissue destruction caused by nutritional and circulatory disturbances which may be accompanied by secondary purulent demarkation and simple or purulent softening. Toxins must be active, such as those of typhoid fever, analogous to the necroses in the mesenteric nodes and intestinal follicles produced by specific bacterial toxins. The foci may be absorbed and heal with superficial contraction. Arterial occlusion by embolism is infrequent; more often there is local venous thrombosis (Ponfick). In other cases, hyalin degeneration of small arteries or occlusion of numerous finer vessels by infectious matter causes death of tissue with perhaps added suppuration. Oppenheim describes a specific nodular endophlebitis as the essential cause of infarcts in typhoid fever.

**Chronic Inflammatory Splenic Tumor. Chronic Inflammatory Hyperplasia**

Among the chronic splenic tumors (splenomegalies) must be considered the inflammatory enlargements of cirrhosis of the liver, syphilis, tuberculosis, malaria, kala-azar and other tropical diseases, the congestion spleen, the progressive hyperplasias of leukemia and pseudoleukemia, (see pp. 235 and 236), and others (see p. 237). Chronic inflammatory splenic tumors occur in two forms. In one (*a*), the hyperplasia is principally of the pulp, but the follicles also participate; the spleen enlarges and retains a normal or slightly firmer consistency. The congestive hyperemia in acute splenic tumor recedes, and the organ becomes paler.

Many splenic tumors remain in this state constantly, or for a long time, with the capsule thickened.

In others there is a transition into the second form (*b*), characterized by hyperplasia of the splenic stroma, with less enlargement, but with thickening and induration (fibrous induration, indurative splenitis). The connective tissue hyperplasia which involves capillaries, vessel sheaths, the larger strands of connective tissue and the finer reticulum may become pronounced enough to cause partial atrophy of the cellular

constituents of the parenchyma, especially of the pulp, while the enlarged follicles are more prominent. The vessels are especially easily seen in the beginning. Later on, the normal architecture of the enlarged follicles and pulp is more and more obscured.

Enlargement is less than in *a*, but the consistency is firmer, often fibrous. The fibrous scaffolding shows prominently; on the smooth section surface the pulp shows vari-colored marbling with dark and lighter colors alternating. Adhesive perisplenitis is present.

Occasional syphilitic splenic tumors depend on hyperplasia of the stroma (see chap. VI). The malaria spleen may belong to the type *a*, but it changes shortly into type *b*.

The malaria spleen may be taken as the type of chronic infective splenomegaly. An acute attack of malaria produces a soft hyperplastic swelling which is differentiated from other acute hyperplasias only by the excessive pigment content, especially in the malignant forms of malaria (p. 210). It is carried by leucocytes, or floats free in the blood, and then is deposited in the pulp and follicles, mostly around vessels. Malarial parasites can be found free or within erythrocytes in the pulp, but most of them are in the reticulum cells which have rich protoplasm and pale nuclei. The plasmodium is usually in rounded form with pigment granules heaped up, suggesting a nucleus.

But in chronic malaria, the spleen steadily hardens, grows larger and becomes red or grayish brown or slate colored to black gray like graphite (black spleen). Progressive thickening of the fibrous network finally overcomes the pulp hyperplasia. The malarial spleen, usually 1000 gms. in weight (ague cake), frequently becomes floating (see p. 221). During regression under quinine therapy the free cells may disappear, but the fibrous induration remains. The spleen may then be even smaller than normal, but remains very hard, and contains, both in the capsule and within, much pigment deposited within the enlarged rounded reticulum cells and sinus endothelium.

It was formerly assumed that the spleen acted as an incubator for the malarial organisms, and that from here periodic invasions occurred accompanied by attacks of fever (intermittent fever). But it is now known that cyclic recurrence is caused by the invasion of fresh erythrocytes by the merozoits (see p. 209). The necrotic wedges mentioned on p. 234 are met in the malaria spleen. They are of scar tissue and retract the splenic surface with capsular thickening. Rupture, frequent in malaria from increased vulnerability, is mostly traumatic; according to Glogner, (Massari, Vorwerk, lit.), it is a typical malarial injury (see p. 232). But the trauma may be so slight, even pressure during vomiting, sneezing, coughing, etc., that it has been spoken of as "spontaneous

rupture." [For the spleen rate as a measure of malaria prevalence, see Coogle, C. P., Pub. Health Reports, Vol. 42, p. 1683, 1927.—*Translator.*]

Tropical splenomegaly with fever which runs a chronic course and is accompanied by anemia, leucopenia, edema, skin hemorrhages and enlargement of the liver is called kala-azar in India and is caused by trypanosome deposits in the spleen (Leishman, Donovan, Marchand and Ledingham, and others, lit. in appendix). The infantile form of kala-azar is also observed on the shores of the Mediterranean (Junesia, Calaprea, Sicily), and has been seen in Rome (Fulci and Basile). The splenic pulp is infiltrated with blood, the follicles are reduced in number and size, the reticulum is not thickened, except in the periphery. The pulp contains cells which enclose blood corpuscles and pigment, among them distended macrophages of 30 to 35 microns in diameter, which contain the pear-shaped parasites (kala-azar parasites or Leishman-Donovan bodies) which, in addition to a larger main nucleus, have an intensively staining granule (blepharoblasts). Macrophages and parasites may also be found in sections and puncture juice of the liver, principally in Kupffer's cells, in the bone marrow, and in the lymph nodes (endothelium). These bodies are proved to be trypanosomes if cultured on blood agar (see p. 211).

Idiopathic splenomegaly or the so-called large cell Gaucher type, is a rare, usually familial, splenic enlargement, beginning early in life and favoring the female (Brill and others). The spleen sometimes attains enormous size from induration, (weight may exceed 8 kilos). The later stages of the disease are accompanied by enlargement of the liver perhaps to double the normal, but always without ascites. There are attacks of pain in the splenic and hepatic regions, tendency to hemorrhages from the nose, gums, skin, melanosis of the skin with yellow to dark brown discolorations which may, however, be absent, and anemia without characteristic blood findings; icterus is usually absent. The course is very chronic. Microscopically, the spleen contains peculiar large cells rounded, oval or polyangular, with one or more nuclei, and clear, hyalin cytoplasm due to a foreign substance, lately recognized as a lipoid (Marchand). These cells infiltrate the pulp in irregular alveoli, or as strands and columns, or diffusely, and replace the pulp blood spaces, thus obscuring the follicles. It is spoken of as large cell splenomegaly. Macroscopically, white striae and spots are visible on a grayish red background, sometimes in reticular arrangement; larger nodules, from the size of peas to nuts are sharply demarkated, rounded or irregular, speckled red to white yellow with dry necrotic yellow centers. The liver, the moderately enlarged, hardly palpable, lymph nodes and the bone marrow, also contain such white foci composed of heaps of these large clear cells. Without doubt it is a systemic disease of all the blood forming organs and the splenomegaly

is only part of the picture. Naegeli believes the disease is a congenital anomaly (mutation) of the reticulo-endothelial apparatus. Schlagenhauser (lit.), refusing to consider these cells as epithelial (Gaucher and others), or endothelial (Bovaird, Banti and Brill-Mandelbaum-Lipman), thinks them the result of reticulum proliferation in the organs named (Cornil); Risel (lit.) circumspectly says they are possibly derived from the reticulum cells (endothelium) and have a special protein in their protoplasm. Others speak of "endothelial splenomegaly" (Graziani). W. H. Schultze pointed out that the enlarged spleen of diabetic lipemia has lipoids in the large cells of the reticulum of the pulp, while the sinus endothelium remains free. Lutz found the latter also involved. These lipoid cells are identical with the large cells of the spleen of Gaucher's type. Kusonoki found these cells, which are negative to sudan and osmic acid, in varying quantities in the spleen in various diseases. Anitschow saw them in experimental feeding with cholesterin. Aschoff thinks the lipoid accumulations in diabetes and in Gaucher's disease belong to the "xanthelasmic diseases." Usually hemochromatosis is present; there is much iron-containing pigment in the organs mentioned and in the skin and musculature (Risel). The etiology is obscure (see lit. by Rettig, Siegenbeck, van Heukelom and Josselin de Jong, Mandelbaum, Brill and Mandelbaum, Marchand). [Also Knox, J. H. M., Wahl, H. R., Schmeisser, H. C., Bull. J. Hop. Hosp., 28, 1, 1916 and for the lipin content, Wahl, H. R., and Richardson, M. L., Arch. Int. Med., 17, 238, 1916.—*Translator.*]

Other splenomegalies are met in various diseases, such as (1) polycythemia, (see p. 187); (2) aleukemic lymphadenosis, (where lymph nodes are not enlarged); (3) aleukemic myelosis (see p. 205); (4) anemia pseudoleukemia infantum (myeloid splenic metaplasia, see p. 193); (5) hemolytic anemia with icterus, (see p. 192); (6) isolated splenic tuberculosis; (7) cirrhosis of the liver, (p. 224); (8) pericardial pseudocirrhosis of the liver, (see under liver); often in (9) chronic portal obstruction (see under liver); (10) Japanese schistosomiasis (see parasites under intestines); (11) rarely in isolated lymphosarcoma; (12) and isolated lymphogranuloma.

### Progressive Hyperplasia of the Spleen

The largest chronic splenic tumors are found in the leukemias, the largest of all, in the myeloid type. The spleen may weigh 4, 6, even 10 kilos at the heighth of the disease. The macroscopic appearance varies (see under blood, p. 198).

In the earlier stages of the disease, the enlarged organ is still fairly soft in consistency, pale, grayish red to lively bright red or flesh colored, quite

homogeneous and pulpy on section or showing washed out, light spots on a pale red background without a trace of follicle demarkation; in other cases the splenic tissue, swollen as a whole, shows densely distributed white, whitish red and whitish yellow nodules the size of peas or larger, which remain with the follicles and are irregular and angular or lobular or leaf-like, following the ramifications of the arteries. Necrotic wedges (p. 234) are prominent on the section surface and may be scattered as yellowish, firm, red-bordered foci (hemorrhages). The capsule is perhaps slightly thickened or is thin and smooth, extremely stretched, sufficiently so, in rare cases, for spontaneous rupture to occur in the form of irregular fissures. The splenic surface at times is uniformly embossed; the spaces between the bosses correspond to the attachments of the resisting trabeculi to the capsule. If the interstitial tissues, *i.e.*, the delicate reticular scaffolding and trabeculae, become hyperplastic, the consistency becomes firmer.

In later stages, hyperplasia of the interstitial tissue progresses until the spleen arrives at a maximum length of even more than 40 cm. This is in myeloid leukemia, but later the organ may become smaller from increasing induration. It is very firm, of almost wooden hardness, very heavy (to 6 kilos and more); on section it is marbled with yellow, yellow brown, brown and black colors. Fresh hemorrhages and pale necrotic wedges due to thrombus formation (a form of white infarction) assist in the picture. Furthermore, the section surface is thickened diffusely or focally almost to the density of cartilage; cicatricial retractions and adhesions to neighboring organs are the rule. The older the tumor, the greater the amount of white calloused connective tissue in the section surface.

X-ray treatment may cause fibrosis (comp. p. 199). In the necrotic wedges are found leucin and tyrosin crystals as a sign of protein decomposition. Charcot-Neumann crystals are also found in the spleen and in the blood and bone marrow of the cadaver.

Histologically, the picture depends on whether it is lymphatic, or myeloid leukemia. The lymphatic form displays enlargement of follicles due to proliferation of small cell adenoid tissue which replaces the pulp; in the myeloid form, a large cell myeloid proliferation (see fig. 130, under lymph nodes) produces myeloblasts, myelocytes and nucleated erythrocytes, cells which otherwise are produced only in the bone marrow; they come from the pulp and displace and crush the follicles. Myeloid change does not occur in the follicles (exception, case of Roman), so that finally the whole organ undergoes myeloid change. The author saw this, among other cases, in a man 41 years old with myeloid (myeloblastic) leukemia; his spleen weighed 2240 gms. The section surface was raspberry red; at the margins were numerous wedge-shaped anemic necrotic foci extending everywhere. The myeloid foci also have iron-containing pigment, for in

this disease, according to Bayer, there are interesting conditions in iron metabolism (see p. 219; also E. Meyer, Heineke, Fabian, Naegeli, Schatiloff). Although the spleen retains plenty of iron, it is not utilized in hemoglobin building; the organ loses its faculty of iron metabolism, and iron excretion in the feces is decreased.

Splenic hyperplasias, less pronounced, it is true, but nevertheless considerable, are sometimes seen in severe anemias, and are quite similar to the first stages of the leukemic spleen; in fact, in this, among other diseases, a myeloid change of the spleen may develop a picture like leukemia. According to E. Meyer and Heineke, and others, this is especially true of pernicious anemia (see p. 191), in which the blood picture may progressively come to resemble myeloid leukemia. All other organs may participate in this myeloid proliferation, according to the authors mentioned, as a compensatory process, by which blood-forming foci are provided to make leucocytes (extravascular) and erythrocytes (intravascular). The occasional marked myeloid metaplasia of the spleen in generalized metastatic tumors of the bone marrow is explained similarly as a vicarious functioning.

The splenic picture in aleukemia or so-called true pseudoleukemia (see p. 206 and under lymph nodes) is essentially the same as in leukemia. As a rule, the more frequent aleukemic lymphadenosis attracts attention to the swollen lymph nodes, while in the rare aleukemic myelosis, the splenic tumor is more spectacular, (in observat. mentioned p. 206, it weighed 1777 gms.).

The spleen in lymphogranulomatosis (see also under lymph nodes) undergoes various characteristic changes. The enlargement is usually moderate (over 1000 gms.), occasionally enormous. As a rule, the lymph nodes, especially the cervical, are also enlarged and it is rare for an isolated large splenic tumor to appear (lit. by Naegeli). In typical cases, the spleen is more or less firm with smooth or roughly granular surface. On section we see inclusions prominent as grayish red, red, grayish white, yellow white to pure white masses often stained with caseous necrotic spots. Their shape is rounded, angular or oval, or, in conjunction with the follicles, plump branching, and nodular, from the size of a pinhead to a pea, of variously dense grouping, and sharply differentiated from the dark red soft pulp. Older cases may show more marked capsular thickening and the general connective tissue of the organ also shows the yellow and brown blotching of the pulp.

The picture is very characteristic, and the organ is spoken of as the porphyry spleen, or, still more descriptively, as the "country sausage spleen." The histology of lymphogranulomatosis may be found under lymph nodes.

## Infectious Granulomatous Tumors

**Syphilis.** In congenital lues, a diffuse hyperplasia, and circumscribed gummata may occur (see under chronic splenic tumor, p. 235), but in acquired lues, the hyperplasia is not constant, indeed, is usually absent. According to Colombini, enlargement of the spleen is observed during the second incubation period, shortly before the appearance of the general symptoms, and the organ grows as the latter come and progress. According to Wile and Eliot, it usually disappears quite soon; in the tertiary stage there is never a splenic tumor worth mentioning, unless perchance amyloidosis or a lobulated liver is co-existent. However, Hubert believes splenic tumor is a very frequent, and with a peculiar paleness of the skin, an important symptom of occult syphilis.

In adults, gummata are rare; they may be of the size of a pea to a walnut, caseous in the center, gray at the periphery, glassy in appearance and seldom numerous. They resemble caseous tubercles, in other cases, old infarctions. It may be difficult to demonstrate their specific character.

In congenital syphilis, the spleen is often enlarged, heavy, hard and reddish brown to blackish red, with the capsule thickened and covered with a stringy exudate. Microscopically, varying pictures are seen; there are diffuse small cell infiltration of trabeculae and vessel walls, increased cellular content and thickening of the reticulum of the pulp, often especially marked in the vicinity of the follicles; in advanced stages, there are marked cellular connective tissue proliferation of all of the stroma, brown granular pigmentation and diminishing size of the follicles; the pulp is poor in cells, and occasionally numerous miliary gummata are found (lit. by Herxheimer). Then the demonstration of spirochaetae is usually not difficult.

The spleen in the newborn weighs about 9 gms. In a 9 months old syphilitic fetus, Birch-Hirschfeld found a spleen weighing 40 gms. The author found them up to 34 gms. Ziegler mentions the exceptional weight of 100 gms. Generally the increase is about to double the normal weight.

In the differential diagnosis, it is well to keep in mind the quite considerable splenic enlargement of universal congenital hydrops, a disease characterized by erythropoiesis, *i.e.*, myeloid tissue formation in many organs, as first described by Schridde (comp. p. 205). The spleen is dark blue red, or brown red, and the normal structure is more or less lost. The cellular mass, diffuse or composed of larger and smaller localized groups without follicles, consists of myeloid tissue (erythroblasts, myelocytes, myeloblasts), and contains much blood pigment (finely granular, without iron). In the liver there is abundant pigment with the iron reaction, which is absent in lues, and blood-forming foci appear in much greater

number than in other fetuses of similar age whether syphilitic or not. The blood shows many erythroblasts; the hydrops is considered a result of the anemia. The cause of this affection is supposed to be a maternal toxin which disturbs the fetal blood formation (see W. Fischer, Loth, Rautmann, Luiz, Lahm, Wienskowitz, lit. Chiari). Such cases have often been mistaken for lues, especially since almost all are born prematurely in the 8th month.

**Tuberculosis** is very frequent and almost always secondary. For differentiation, there is a fine nodular form—acute (*a*), and a large nodular, more or less chronic form (*b*).

(*a*) Acute miliary tuberculosis of the spleen is an almost constant finding in general hematogenous tuberculosis. The spleen may increase

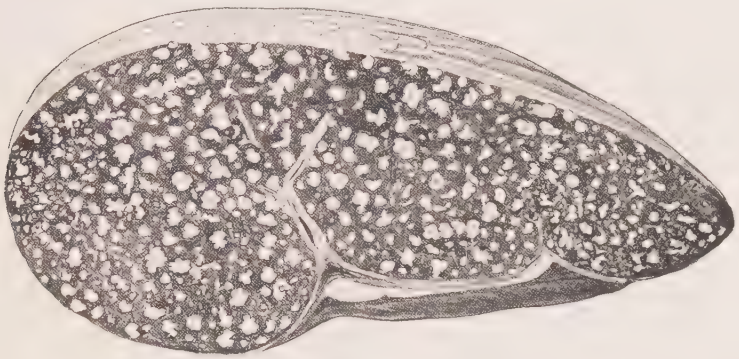


FIG. 121.—Miliary tuberculosis of spleen; weight 107 gms.; miliary, submiliary and supermiliary tubercles and conglomerate tubercles stand out sharply from the dark red surface. Fibrous tuberculous perisplenitis; 1 year old boy with general miliary tuberculosis, caseous pulmonary tuberculosis with tubercles in veins. Nat. size.

quite considerably in size and weight; it may be firm or soft. The section surface, usually deep red or reddish brown in color, shows numerous, scattered miliary (size of millet seed) or smaller (submiliary) tubercles, sharply circumscribed, and gray or grayish red, or grayish yellow in color. Sometimes the minute tubercles are so thickly scattered that the section surface appears finely granular and has a granular feel. In other cases the dissemination is less wide spread, but then the discrete tubercles are more voluminous, *i.e.*, truly miliary, or larger and gray with caseous centers. On the surface, innumerable tubercles can be seen and felt; they may have red borders. Sometimes there are fibrin deposits covering tubercles in the capsule (fig. 121). The macroscopic differences between miliary tubercles and follicles:

Tubercles are unequal in size, irregular, unevenly scattered and usually more thickly strewn than the follicles; they are usually smaller, although isolated tubercles may be larger; they are more prominent and

more sharply outlined than follicles. Sometimes they are surrounded by a red zone. They are grayish yellow and translucent like sand grains, while follicles are grayish white and cloudy. Tubercles are firmer and harder, and may be lifted out of their beds with the knife point, while follicles tear and disintegrate. In children, the latter are always more prominent and closer together than in adults so the differentiation is more difficult. Microscopically, the tubercles are lymphoid and epithelioid, usually with giant cells; they are frequently caseous. They may be scattered anywhere in the pulp, follicles, trabeculae, or under the capsule. Tubercles frequently fuse. They vary markedly in size (see Heitzmann, red blood cells in miliary tubercles).

(*b*) Subacute and chronic tuberculosis of the spleen.

Larger caseous areas are found in spleens otherwise little changed, or only moderately enlarged. These areas consist of globular conglomerate tubercles, possibly the size of lentils to cherries, often with small nodules at the periphery; they bulge like tumors and form bosses on the surface (nodular form), or larger areas to the size of beans are sometimes wedge-shaped, packed with tubercle bacilli and caseous (infiltrating form). Sometimes the nodules, rosette shaped, change by central liquefaction into cavities with cheesy walls and creamy contents.

Occasionally the tubercles quantitatively exceed the splenic parenchyma. The author has seen large nodular splenic tuberculosis which resembled the "porphyry spleen" of lymphogranulomatosis (see Ceelen and Rabinowitsch), and the reverse as well (p. 239).

Chronic tuberculosis is most frequent in "scrofulous children," in whom indeed, the largest tubercles are found. But the author saw many nodules almost as large as chestnuts in a female phthisic 51 years old with intestinal ulcers and numerous liver tubercles the size of cherry pits (autopsy 113, 1906, Basle). In a 53 year old woman, the spleen weighed 465 gms. and from the soft, dark red pulp, cherry sized, fairly firm, reddish gray, glassy nodules with yellow caseous inclusions were present in large numbers (aut. $95^{11}/_{12}$). Similar nodules were found in the liver; tuberculosis of lymph nodes and scars in the apices of the lungs were coincident. Numerous, large nodular tubercles are frequently seen in guinea pigs used for experimental purposes, as well as in monkeys which are much more susceptible to human tuberculosis than to the bovine type (see Cindemann). Occasionally children, more rarely adults, show similar pictures (so-called monkey tuberculosis).

Primary tuberculosis of the spleen has been infrequently described, and many cases are doubtful (lit. by Pertik, J. Bayer, Banti). Huge splenomegalies have been described with large cheesy tubercles, others with miliary tubercles; others, *e.g.*, the cases of Carbone and Auche

(spleen 1250 gms.), showed intense increase of connective tissue with destruction of follicles, necrosis and tubercles. In the last two cases there was also cirrhosis of the liver, which, according to Carbone, was analogous to that in Banti's disease (p. 224) (lit. by Sotti, with remarks about hyperglobulia, p. 187, in primary tuberculosis of the spleen; this hardly can be considered a causative factor in hyperglobulia—see Jung; see Wiedwald and Winternitz lit.).

In *glanders* the spleen may show small nodules of hematogenous origin.

In *leprosy*, miliary, yellow and brown nodules may appear (see Biehler).

In *actinomycosis*, metastatic foci are rare (see Abee and comp. under liver), but the spleen may be constitutionally affected (see, for instance, Kramer).

### Degenerations

**Atrophy.**—In senile atrophy, the spleen is smaller, tougher, and brownish in color, the capsule is slack, wrinkled and thickened.

In malnutrition such as in marked anemia, cachexia, carcinoma, etc., simple atrophy is less constant. The organ becomes pale red and flabby.

In 1078 cases of carcinoma, the spleen was enlarged in 35.3%, but usually from obstruction (see Marschoff I. D. Basle, 1907, lit.). While the cellular elements of the pulp, *i.e.*, the splenic substance, decrease (pulp atrophy), the trabecular scaffolding and vessel sheaths are relatively prominent and usually thickened. The follicles likewise become smaller and impoverished in cells. For details in reference to follicular involution processes, see Groll and Krampf. The adventitia vessel sheaths contain, like the pulp, amorphous, brown intracellular pigment.

In the most extreme cases, the weight may drop below 20 gms., the spleen is no larger than a walnut. The collection at Basle contains a spleen weighing 19 gms. coming from an 82 year old woman of 25 kilos body weight. At Gottingen, there is one 10 gms. in weight, from a 62 year old woman.

**Amyloid Degeneration, So-called Amyloid Infiltration.**—Amyloid is exceedingly frequent in the spleen in the conditions discussed more in detail under amyloid liver. See there in reference to amyloid reactions.

Differentiation: In the sago spleen, the follicles are attacked. Amyloid degeneration affects chiefly the reticulum, small arteries and the capillaries of the follicles. The fibres of the reticulum swell into sausage-like, clubbed, or varicose, glassy strands narrowing the meshes of the adenoid tissue into angular or stellate spaces containing a few lymphocytes fiig (122).

More detailed investigation has shown that the fibres are first covered with amyloid and soon die, which naturally precludes swelling (Ebert).

Not rarely, the parts of follicles around the axial artery remain free of amyloid. Macroscopically, the follicles project like grains of sago or fish eggs, as gray, translucent nodules above the section surface. Application of a solution of iodine stains the amyloid follicles mahogany red. Minor degrees cannot be recognized macroscopically. The spleen is never very large, (rarely 500 gms.); it may be pale red and much harder than normal.

The ham-, bacony-, or waxy-spleen contains amyloid of the pulp or of both the pulp and the follicles.

In more advanced stages, clumps of hyalin amyloid are deposited between the trabeculi; the reticulum fibres are thickened and the pulp cells pushed aside. Arterial capillary and venous walls become hyalinized, some vessels resemble sausages, and the lumena are occluded. Amyloid is grayish white and glassy in unstained preparations. Without the iodine

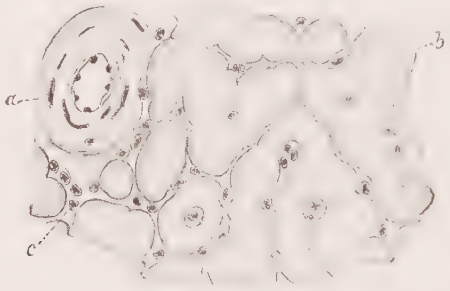



FIG. 122.—Amyloid degeneration of spleen; portion of a follicle. a, Small artery; b, reticuum fibers; c, lymphocytes in the narrowed meshes. Hematoxylin-eosin stain (high power).

reaction, these two forms cannot always be differentiated macroscopically, since, especially in advanced amyloid of the pulp, the follicles are atrophic. The section surface is smooth, homogeneous and glassy with distinct trabeculi, but only microscopically can we see that the follicles are atrophic and not infiltrated by amyloid. The spleen is enlarged, more in thickness than in length, is stiffened, plump, and has rounded edges. Its capsule is smooth, tensely stretched, and perhaps very thin. Its specific gravity is increased. The consistency of the peculiarly dry parenchyma is firm, doughy, or stiff, and in marked degeneration, actually hard, not yielding to pressure. Alcohol fixation increases the hardness. The color, apart from the blood content, is red, like smoked ham or salmon, or pale, brownish yellow like wax or boiled bacon. Fairly thick slices of a waxy or bacony spleen are transparent if cleared in glycerin, so that only the trabeculae and follicles are opaque and therefore plainly visible.

W. Fischer mentions as a frequent finding (9 times in 16 cases) the presence of foreign body giant cells at the edge of tissue showing amyloid degeneration, which Krawkow had already observed in experimental

amyloidosis of the spleen. Tsunoda, however, found it but twice in 35 cases, and he warns against mistaking them for tubercle and pulp giant cells.

See Strada, for spontaneous rupture of the spleen in amyloid disease.

**Perisplenitis—Parasplenitis.**—The first is an acute or chronic inflammation of the splenic capsule which is covered by peritoneum. It arises from without (*a*) or from within (*b*). In the latter it follows abscesses (see p. 233), infarcts, chronic hyperplastic and indurative splenitis, and echinococcus disease; while in the former, it may be part of a general or local peritonitis extending from the neighborhood (stomach, colon, left kidney, pleura). The fibrinous exudate covering the surface is organized into fibrous and membranous adhesions to the vicinity, (adhesive perisplenitis), or fringes, or flat warty nodules, or calloused smooth elevations, often cartilaginous in consistency. Hyalin-fibrous plaques and scales, mostly on the convexity of the organ, cover it as a shield or shell, but occasionally like a thick, smooth porcelain casing (zuckerguss spleen). If the organ is completely surrounded, it undergoes atrophy (chronic fibroplastic perisplenitis). Sometimes firm fibrous strands, following the trabeculae, continue between the superficial layers of the parenchyma. The fibrous tissue may hyalinize and calcify. Small hemorrhages occurring in the peritonitis leave spotted brown pigment patches in the capsule.

Parasplenitis, an inflammation around the spleen, may also have its origin within or without (stomach, colon, etc.). If between the spleen and diaphragm, it is called "subphrenic abscess" (see p. 233).

**Tumors and Parasites of the Spleen.**—Primary tumors are infrequent. Occasional fibromas, chondromas, osteomas, lymphangiomas (cavernous, at times multiple—Barbacci), have occurred (see fig. 123). At the lower pole of the spleen of a 32 year old woman the author saw a cystic lymphangioma the size of a fist; it was lined with flat endothelium containing clear, slightly yellow fluid with numerous fat droplets. See polycystic lymphangioma, so-called polycystic degeneration, by Fink, Coenen, Fibiger. The rare cavernous hemangiomas, so-called cavernomas, are usually small; the author saw one the size of a cherry slightly bulging on the splenic surface. They may be multiple (Stamm, Albrecht, Strada, v. Benckendorff, lit. Anzilotti, Geipel). When there are many angiomas, the condition is spoken of as hemangiomatosis; it possibly involves the liver also (metastasis?, Langhans). Ernst and v. Falkowski (lit.), saw multiple blood vessel tumors in the spleen and liver together with angiomatosis of the skin, which they interpret as mesenchymal hamartomas due to a slowing of the embryonal mesenchyme in differentiating into vessel wall cells, connective tissue and blood components. The marked endothelial proliferation can easily be mistaken for endothelial sarcoma.

Hedinger (Pentmann), in a case with cavernous formation, saw a diffuse proliferation (hamarty) of blood vessel endothelium which remained passive, *i.e.*, did not develop into vessels, within the immensely enlarged spleen and liver. Sarcomas are quite rare; among them have been found round or spindle cell varieties (lit. by Simon, Bunting, Prinzing), sarcomatous angiomas, *i.e.*, endothelial sarcomas, etc. (Theile, Jores, Risel, Golovina-Ammon.)

Small cysts are not rare, but are unimportant (at most 1 cm. in diam.): they show prominently on the surface, are sometimes conglomerate or like strings of beads, especially along the anterior edge, reaching somewhat into the spleen. They are considered by M. B. Schmidt to be dilatations of lymph vessels. The formation of these cysts is always combined with minute ruptures of the capsule, which leads to small red projections, the so-called splenic tissue hernias, or to prolapse of the pulp through tears in the capsule and subsequent cavities. Such hernias and prolapses of splenic parenchyma may also result in marked splenic swelling without cysts. Von Ramdohr and Beneke, on the other hand, suggest a more plausible explanation; multiple capsular ruptures lead to hernial bulgings of the pulp, the peritoneum becomes enclosed in these bulging splenic tissue masses, the hollow spaces and clefts are dilated by secretion (see Zieglwallner and Wohlwill, lit.). But according to Jamashita, and P. Muller also, the lymph vessels must be considered; splenic hernias may lead to obstruction of the outflow of lymph, and even of veins, making the condition really one of lymph- and hemangiectasis, with the cooperation of the peritoneum in the formation of serous cysts wherever the hernias touch. Renggli, (see also Kuhne), believes that in his case there was fusion of fringing projections lined by peritoneal cells all outside the capsule (extracapsular cyst), and Welti, in a similar case, assumed there was an extrauterine snaring-off of peritoneal epithelium. Large true serous or sero-sanguinous cysts are very rare, likewise pseudocysts. The latter are frequently of traumatic origin or are liquefied non-infected infarcts. For the so-called blood cysts, see lit. by Jordan, Suchanek, Hedinger, Solieri, Fossler. For a very rare splenic dermoid, see Kumaris. [For a tuberculous cyst, see Peck, C. H., Surg., Gyn. & Obst., 162, 1924.—*Translator.*] Secondary tumors are also infrequent. Sarcomas are the most common, especially the round cell variety, next lympho- or melanotic sarcomas which may fill the whole organ with brown and black to coal black, rounded nodules. Secondary carcinomas are much rarer. In the material at Basle, among 1078 carcinoma cases, only 0.7% were seen with metastasis in the spleen, one each from carcinoma of the uterus, rectum, stomach, penis, breast, gall bladder, kidney and a chorioepithelioma of the uterus (see I. D. Marschoff). This is explained by the tend-

ency of carcinoma to spread through lymph channels; metastases reach the spleen only by the blood route. Larger carcinomatous nodules, often numerous, are seen practically only in general disseminating carcinomatosis, in which viable carcinoma cells enter the greater circulation and thus the blood of the splenic artery. But, first described by the author, retrograde distribution into the spleen through the veins can also occur. It happened in a platter-shaped ulcerating, posterior, gastric carcinoma in a 60 year old woman. The tumor filled not only the trunk of the splenic vein, but continued throughout the whole organ, expanding in the venous sinuses to the size of cherries. Thrombotic masses could be lifted from the cavernous cavities; there were metastases in the liver, and a

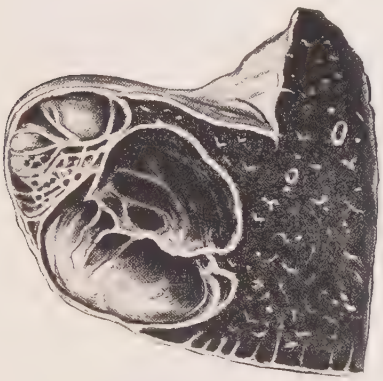


FIG. 123.—Cystic lymphangioma of spleen. The contents coagulating like jelly in formalin, light gray in color, were removed; 49 year old man. Nat. size.

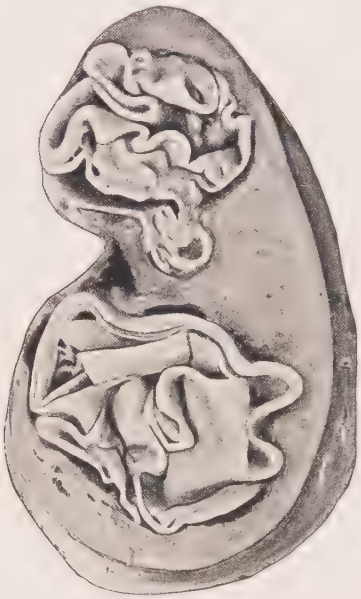


FIG. 124.—Echinococci in spleen of a 12 year old girl. Two cysts filled; 7/8 nat. size.

single, flat, nodular one in the fundus of the gall bladder (no calculi). Less extensive vessel occlusion by retrograde distribution was seen by the author in a 50 year old man with gastric carcinoma (see also Geipel, Parsch, Chalatow). Occasionally an infiltrating carcinoma of the vicinity (stomach, intestine, pancreas) extends to the splenic surface and coats it with tumor tissue; then the lymph channels are also utilized for dissemination and a retrograde extension can start from the hilum into the organ through these vessels in the trabeculae (Geipel).

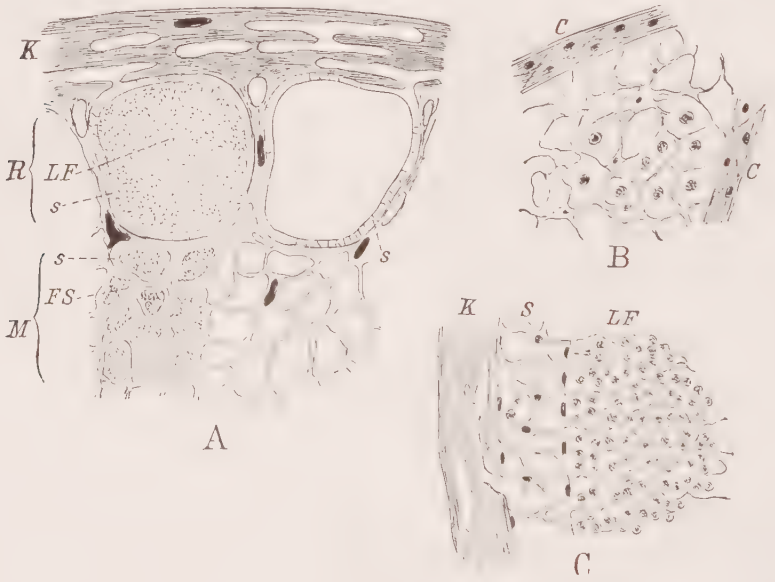
It is true that microscopic carcinomatous metastases in the spleen are not so rare, (v. Hansemann, Deelmann), but the paucity of macroscopic, visible nodules proves that many carcinoma emboli perish in the organ. Chalatow, for instance, found no signs of proliferation in these micro-

scopic metastases. This suggests some immunizing property of the spleen with reference to animal tumors, see Schmincke, lit.

**Parasites.**—Cysticercus is rare, while echinococci are more frequent with central or peripheral situation. They may become exceptionally large, causing almost complete disappearance of the parenchyma. Not rarely the echinococci are found in other situations as well, in which they are more frequent, and in the liver, mesentery, or elsewhere in the abdominal cavity. Pentastomum (see under liver) may form calcified nodules to the size of a pea, and have been mistaken for phleboliths. [For hydatid cysts of the spleen, see Mills H. W., Surg. Gyn. & Obst. 491, 1924.—*Translator.*]

## LYMPH NODES

**Anatomy** (see figs. 125 to 127).—Lymph nodes are bean-shaped and have a smooth, quite homogeneous, section surface. They are enclosed




Figs 125–127.—Free after Klein { A Lymph node, diagramatic, see text. B Adenoid tissue, C.C. Capillaries. C Portion of edge of lymph node. K, capsule with afferent vessel; S, cortical sinus; LF, portion of lymph follicle.

in a fibrous capsule, the outer layers of which always contain fatty tissue. From the capsule, dividing walls enter the parenchyma separating it into spaces, larger and rounded in the outer third or cortex, and smaller, narrow and cylindrical in the inner parts or medulla. The meshes all intercommunicate and are filled with adenoid tissue, with the exception of a peripheral space (sinus).

The lymph adenoid tissue constitutes a reticulum of fine, homogeneous fibrillae with cellular flat thickenings in its knots. It has numerous capillaries starting from an artery, and continuing into a vein. The reticular meshes contain lymphocytes consisting of a nucleus, rich in chromatin, and very little cytoplasm. (For screen fibre scaffolding, see Rossle and Yoshida.)

The cortical adenoid tissue corresponding to the framework in which it is contained, is in the shape of oval or globular masses, the so-called lymph follicles, or cortical nodules, while the medulla is composed of follicular strands. Many follicles show lighter centres, poor in cells, the so-called germinal centres (fig. c), with larger lymphoblasts which are supposed to give rise to the small lymphocytes, but Hellman (lit.) thinks that these "secondary" follicles (light areas with dark peripheries) are reaction centres caused by irritative products from bacteria or other toxic bodies and substances. There is always an empty peripheral space between the adenoid tissue and the scaffolding. This is the lymph sinus or perifollicular space which surrounds the adenoid tissue like a moat and contains lymph and lymph corpuscles. Those just below the capsule are called border sinuses (fig. c), but all the sinuses in the cortex and medulla communicate, forming a labyrinth. In the sinus itself there is also a relatively coarse reticulum sparsely supplied with endothelial cells. The fibres are thicker than those of adenoid tissue (fig. c) and the endothelial cells which cover them are called reticulum cells. They have storage powers, and according to Askanazy, are the chief factors in filtering and blood cleansing. The lymph sinuses, lined with endothelium, are direct prolongations of the afferent lymph vessels.

**Circulation of Lymph.**—Since the afferent lymph vessels break up in the capsule into a thick network of branches, the stream passes into the cortical, then into the medullary sinuses and from there into the efferent vessel in the hilum of the lymph node. In its passage the current is much retarded.

If a lymph node is drained from the afferent vessel by a cannula or from beneath the capsule by a Pravaz syringe, the sinuses empty first; then with further rinsing, the lymphocytes are washed out of the peripheral parts of the follicular substance.

**Blood Vessels.**—Arteries and veins pass into, and out of the hilum. The arteries are lost in the follicular substance, where the veins start.

**Physiology.**—The follicles supply lymphocytes which pass both through the lymph sinuses into the efferent vessel, and into blood capillaries. Naturally, the conception "lymph gland" is not that of a true gland *i.e.*, an epithelial structure which supplies a secretion. Lymph nodes function as coarse filters, which is possibly more important. The sinus endothelium, like the reticulum cells, (see above), possesses phagocytic

properties against substances in solution and fine particulate elements such as fat droplets, erythrocytes, soot, bacteria, etc. (see Stheeman, Holthusen, and next chapter). Indeed, it is believed that their chief function is blood purification (see Askanazy). They are part of the so called "reticulo-endothelial apparatus," which has similar functions, and is composed of reticulum, endothelium, and hematopoietic tissues, (bone marrow, spleen, lymph nodes, liver; see p. 219).

The number and structure of the lymph nodes vary at different periods of life, (see Hellman, the quantity of lymphoid tissue at various ages, and lit. in ref. to lymphoid tissue in general). In the new born, the number is very large, but decreases with age. The same is true of the diameters and numbers of lymph vessels. Cells predominate in the young; in middle age, connective tissue fibres become more prominent, and elastic fibres appear. In senility, the cells are relatively few in number, the connective tissue is thickened and the elastic fibres splintered (T. Bartel-Stein).

In addition to the typical lymph nodes there are others called hemolymph nodes, (see Weidenreich), scattered along the blood circulation. Blood from permeable capillaries enters their meshes (which contain lymphocytes), and is collected in the veins after phagocytic destruction of erythrocytes by the lymphocytes and endothelium, (lit. in appendix).

### Generalizations in Reference to Diseases of Lymph Nodes

Most diseases of lymph nodes are secondary, and lymphogenetic in nature. Since all evidence points to the lymph nodes as filters, and since foreign substances, innocuous and injurious, are constantly added to the lymph, the frequence and variety of contamination of the lymph nodes are often of grave consequence.

These may be dead particulate elements, (dust, especially soot and coal, coloring matter, disintegrated blood cells, etc.), living tissue cells (red and white blood corpuscles, tumor cells), bacteria, for which, however, the filter is not always sufficiently impermeable, (see Kovacz, Noetzel), and their metabolic products, inflammatory products (exudate, pus, etc.), and chemical poisons. The substances mentioned may be retained permanently, or merely for a time, to pass on after injuring the parenchyma, causing inflammation, degeneration, necroses, etc.; or, they are made harmless or destroyed, probably a frequent happening with infectious material, since the lymphocytes, and more especially, the endothelium act as phagocytes. According to Hellman, benign coal particles reach the medulla promptly, while carcinoma cells and tubercle bacilli are first held by protective processes in the peripheral parts.

The lymph node thus loses its integrity, at times even its existence, in endeavoring to protect the whole organism.

The relation of diseased regional lymph nodes to primary disease within their drainage area is observed in acute and chronic inflammations, and in tumors, especially carcinomas (p. 283). The axillary nodes swell from even a small infected wound of the hand or arm. As other examples, we may mention swelling of the maxillary and cervical nodes in diseases of the mouth, (dental caries), and of the larynx, (angina, scarlet fever, diphtheria); swelling of the inguinal nodes in male sexual affections; of the bronchial nodes in pulmonary affections; of the mesenteric nodes in intestinal affections, especially tuberculosis and typhoid fever. The disease may extend from one place to another, and if the way is blocked in one direction, another, even retrograde route, may be used, (p. 184).

Other secondary lymph node diseases are hematogenous in origin, involving several, and in rare cases, all lymph nodes simultaneously, in contradistinction to the lymphogenous processes which usually attack isolated nodes. They are much rarer than lymphogenous diseases, and appear chiefly in general infections such as scarlet fever, diphtheria of the pharynx, etc.

As distinguished from these secondary involvements of known etiology, the primary, idiopathic, spontaneous changes in lymph nodes, *i.e.*, the hyperplasias and true tumors (frequently very malignant), are rare and their origins are more or less obscure (infectious cause? see p. 271).

### Inflammation of Lymph Nodes. Lymphadenitis

**Acute Lymphadenitis.**—In simple hyperplastic lymphadenitis, the nodes are enlarged and juicy, the capsule is tense, and the blood vessels injected. The consistency is at first soft; a grayish red to dark blue red pulp can be scraped from the section surface. Then a marrow-like change takes place, especially in typhoid fever, the color becomes gray to white, and the architecture is indistinguishable. The general moisture of the surface is gradually diminished. This is easily mistaken for caseation or carcinoma.

The color change is due to the displacement of the hyperemia by an increasing multiplication of the cells in the follicular substance. The participation of sinus endothelium is remarkable; it proliferates, swells, desquamates, regenerates, and may lie partly free in the sinus, (desquamative catarrh of the sinus). It, like the reticulum cells, supplies phagocytes. The lymphoid cells in the sinus are also increased; both leucocytes and fibrin flakes may be seen within. All this is hyperplasia, and the outflowing lymph shows greater abundance of cells.

The process may regress at this stage; the excess cells undergo fatty degeneration, or are removed through the sinus. After a short period of

hyperemia, there is restitution and perfect repair; but a chronic inflammation, pus formation, or, (as in typhoid fever), necrosis, may ensue.

Purulent lymphadenitis may follow the simple adenitis described above, but only when pyogenic organisms are present. Yellow spots in the juicy lymph nodes gradually assume the consistency of pus, (abscesses), coalesce, and form cavities with sanguino-purulent contents.

Microscopically, the sinus shows desquamated, fatty degenerated endothelium, fibrin, and leucocytes. Follicles and strands are so completely packed with pus cells (polymorphonuclear leucocytes) that the reticulum melts away. During this disintegration, the injected blood vessels are eroded, ragged, and allow hemorrhages into the pus. An abscess may involve the entire lymph node and extend to the vicinity (periadenitis) as a phlegmon, *e.g.*, the inguinal buboes of soft chancres (see under skin). If the node is near the surface, external perforation occurs, occasionally through cribriform openings from several foci, or into a neighboring empty space, *e.g.*, from bronchial nodes into a bronchus or the esophagus. The purulent periadenitis then causes necrosis or sequestration of the remaining lymph tissue by surrounding it with pus and destroying its nutritive vessels.

Small abscesses may localize and heal. The pus undergoes fatty degeneration, is absorbed, and scar tissue is deposited; or the pus thickens, is infiltrated with lime salts and becomes hard like mortar or stone. Under these conditions, a sort of capsule is formed by connective tissue proliferation. If the whole node has suppurated, its site becomes a hard cicatrized nodule after all dead material is removed.

Suppurative lymphadenitis (purulent bubo, see under skin) is a complication of soft chancre in a large percentage of cases, but may result from other infected wounds, especially those acquired at autopsies, from severe suppurative tonsillitis, diphtheria, etc.

**Rarer Forms of Acute Lymphadenitis.**—Fibrinous exudation is frequent in diphtheria; the cervical nodes are infiltrated by leucocytes, and networks of fibrin threads appear in the sinuses, follicles and blood vessels; the same exudation occurs in pneumonia. Necrotic foci, *e.g.*, in typhoid fever, may likewise contain much fibrin. In addition, fibrino-hemorrhagic exudations occur in glanders and bubonic plague, and are especially characteristic of anthrax, in which the bacilli can usually be found.

**Necrosis.**—Slight necrosis within the follicles (in the spleen also) is seen in diphtheria, scarlet fever, and around clumps of bacteria in suppurative lymphadenitis. It is of little importance except in typhoid fever, in which the necrosis is focal in the cellular tissue, hyperplastic from the specific action of the typhoid bacilli clumped in fairly large masses. This is

analogous to the conditions in the follicular apparatus of the intestines. The lymph nodes are usually those near the cecum, (ileo-cecal) or anywhere in the mesentery. The necrotic masses may soften, become secondarily infected and rupture into the abdominal cavity, causing a peritonitis, generally fatal.

In other cases, the necrotic fluid inspissates and is calcified, and when found later may be mistaken for tuberculous remains. (Many interpret all calcified nodules as tuberculous, see Naegeli.)

Ichorous liquefaction is seen occasionally in scarlet fever and diphtheria, but much more frequently with the hemorrhages and suppuration of bubonic plague in which the inguinal, crural, axillary and cervical nodes are more frequently affected. According to Crowell, the most characteristic change is edema of the periglandular tissue. Plague buboes often rupture. Clinically, three forms of plague are distinguished, the bubonic or lymph node, the pustular and carbuncular, and the pneumonic type. The disease is transmitted by fleas from rats to humans, (see Kitasato, Kisskalt, van Loghem and Swellengrebel). Plague bacilli may be obtained from the buboes (Kitasato and Yersin).

**Chronic Lymphadenitis.**—Simple, in contradistinction to specific, tuberculous, or syphilitic, chronic lymphadenitis is due to repeated, or long continued irritation of the tissues. It is also spoken of as simple secondary lymphoma in contrast to the specific and primary forms. The clinician calls all chronic and tumor-like enlargements of lymph nodes, lymphomas, but this name should be confined to the primary hyperplasias.

The irritants may be (*a*) organic causes (bacteria), (*b*) chemically active substances introduced and carried through the lymphatics, and (*c*) mechanical irritants such as dust particles carried by the respiration into the bronchial nodes.

The changes in the lymph nodes vary:

In chronic hyperplasia, all parts are increased and the architecture remains essentially intact. There is merely enlargement and induration, the latter due both to greater filling of the reticulum meshes and to thickening of the trabecular scaffolding.

In other instances, fibrous induration and inflammatory connective tissue production occur in the capsule as well as in the coarser and finer trabeculae, while the cellular elements, including the fine reticulum, undergo atrophy. The endothelial cells are small and spindle shaped; the connective tissue becomes hyalin and sclerotic. This form develops especially often in the bronchial lymph nodes; long continued dust inhalation (anthracosis) causes considerable enlargement of the slaty, indurated nodes. Such a process, as well as the healing of an abscess, may lead to

partial or complete cicatricial atrophy. Indurated lymph nodes are often closely adherent to their surroundings.

### Pigmentation of Lymph Nodes

The bronchial lymph nodes, which are most often involved, frequently show pigmentation (anthracosis), from soot and coal dust-laden inspired air. It may begin in the first months of life. First the sinus endothelium, then the reticulum cells take up finely granular particles of soot. Active connective tissue proliferation with pigment in the cells and clefts leads to gradual atrophy of the lymphoid tissue and finally to more or less complete atrophy of the parenchyma. Anthracosis often causes fibrous induration (slaty or anthracotic induration), combined perhaps with lime salt infiltration, when the lymph nodes are dense, dry, hard, and considerably enlarged. In other cases, a moist, friable, black substance suggests smears of india ink; microscopically, there are pigment, fat granules, cholesterin, lime granules and debris. The pigment may be carried from the bronchial nodes into the walls of the bronchi, trachea, neighboring veins or arteries, and esophagus, after a preceding adhesive periadenitis. Sometimes the parts undergo ulceration and perforation, and dangerous communications between the esophagus and bronchus are established, with subsequent gangrene of the lung (details under lungs and bronchi). But even without rupture, pigment is transported by the blood channels, with or without the help of leucocytes, into other organs such as the liver, spleen and bone marrow (Walz). Other forms of dust (cinnabar-iron-and stone dust) are also found in the bronchial nodes (see under pneumokoniosis). Other forms of pigmentation are:

Tattooing of the skin, in which finely granular substances are rubbed through punctures in the skin (gun powder, cinnabar and other colored matter). At first, the pigment lies in the sinus, later it is imbedded in the endothelial and round cells of the follicles and strands, still later in the stellate and spindle cells of the reticulum.

From red blood cells—after autochthonous hemorrhages, or after absorption of a hemorrhagic extravasation, as from congestion of the lungs and hemorrhagic bronchopneumonia, or from some other cause destructive of erythrocytes. In cases of the first kind, blood is found in the peripheral sinus and the sinus endothelium, which is hyperplastic, exfoliated, and phagocytic to large numbers of red (and white) blood corpuscles (Saltykow). Some of the blood reaches the vasa efferentia. Later, yellow and brown iron-containing granules are found in the lymphoid tissue, especially near the peripheral sinus. This produces brown or slate-colored nodes without induration, just as though the pigment had been introduced, *e.g.*, in gastric ulcer in the epigastric lymph nodes, in intestinal ulcers, in the

mesenteric lymph nodes, etc. The black or gray color is due to the formation of iron sulphide by the action of intestinal gases.

Pigment transport into lymph nodes is occasionally seen in Addison's disease (Riehl), in which the skin assumes a bronze color (see under adrenals). This pigment is brown. In other skin affections also, pigment transport to regional lymph nodes occurs, (Jadassohn), as from a graft of negro skin implanted on white skin (Schmorl).

### Infectious Granulation Tumors

**Tuberculosis of Lymph Nodes.**—Tubercle bacilli enter via the blood as in general miliary tuberculosis, or, more frequently through the lymphatic channels.

While v. Baumgarten, on the basis of animal experiments, thinks that the hematogenous mode of infection is of somewhat greater importance, Joest and Noack, also on the basis of animal investigations, claim that lymphogenous infection is more frequent. Haustein (lit.) supports the claim of v. Baumgarten. In hematogenous tuberculosis, distinct tubercles develop (but few tubercle bacilli are present), while caseation is more pronounced in lymphogenous tuberculosis (mass action with an abundance of toxins, see Tendeloo).

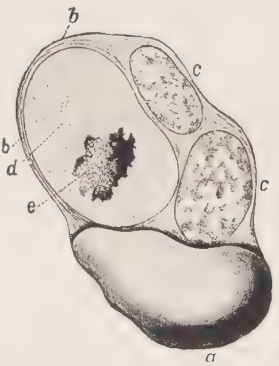



FIG. 128.—Conglomerate caseous cervical lymph nodes. a, Nodule uncut; b, cross section through a completely caseated, almost homogeneous node; c, node with multiple caseation; d, cheesy material; e, cavity due to softening of caseation. From a young adult; ⅔ nat. size.

Tuberculosis appears in various forms:

The many small tuberculous nodules which contain bacilli are strongly staining lymphoid, or epitheloid in nature, and often contain giant cells which stain faintly (see Joest and Emshoff in reference to histogenesis). Macroscopically, early tubercles are tiny, cloudy, firm, gray nodules of miliary or submiliary size, usually in the follicular tissue. Tubercles in the productive stage are accompanied by a soft inflammatory swelling and reddening of the entire node.

Usually this infection is secondary, the primary focus being found in the vicinity, *e.g.*, tonsillar tuberculosis and infection of the cervical lymph nodes (see p. 288).

In their further course, tubercles become caseous, and by peripheral extension and confluence, conglomerate.

The second form begins as a diffuse cellular hyperplasia; there are heaped up innumerable small cells, larger epithelioid cells, spindle cells (fibroblasts), and a few giant cells. The node may be somewhat enlarged.

Ziegler designated this process "diffuse large cell hyperplasia" but it is also called "tuberculous lymphoma," (see note, p. 252).

It was shown in animals by Bartel, and Bartel and Spieler, that ingested tubercle bacilli may pass through an intact mucosa and reach lymph nodes, remaining viable in this situation, but latent, for long times, (in rabbits at least 104 days), without causing any specifically tuberculous tissue changes. They do produce a simple lymphoid hyperplasia, which may or may not precede the specific tuberculous changes.

They called this effect the "lymphoid stage." But the questions are by no means answered, *i.e.*, whether it is proper to speak of lymph nodes as tuberculous while the tubercle bacilli are latent, or to apply these experimental findings to the conditions found in humans.

Joest (lit.) for instance, does not believe there is a lymphoid prestage in animals, and considers the vaccination test in the guinea pig positive only if microscopic tubercles are found in the nodes. Henke-Jonske agree, while others believe the organism can be latent in animals, as well as in humans (lit. Linnenbrink; Weichselhaum, W. and Bartel, Gaffky, see Harbitz, lit. v. Beitzke, 1910, Joest, Bariel). Furthermore, latent tubercle infection of lymph nodes can heal, perhaps leaving a hypersensitivity (allergy) so that in adult years there is a predisposition to new active infection (v. Behring; Bartel, lit.). The course of this second form of tuberculous lymphadenitis varies:

There is a form with an abundance of bacilli which causes quick focal, then diffuse caseation and softening. It is found especially in children. If the gland is completely caseous, the section surface is dry, homogeneous, brittle, cracked, or pultaceous yellowish white (so-called potato glands). Those most frequently affected are the cervical, bronchial and mesenteric chains.

Microscopically, the central parts show diffuse caseation; towards the periphery, the grouping of the individual foci can be recognized as typical tubercles (epithelioid cells, caseating giant cell nodules), caseating epithelioid cell nodules without giant cells, or completely caseated nodules. Sometimes no giant cells are present which makes the diagnosis very difficult.

A relatively benign form is spoken of as "attenuated tuberculosis;" it is poor in tubercle bacilli, and runs a chronic course with a tendency rather to induration than to caseation or softening. The nodes enlarge slowly, occasionally to the size of hen's eggs or kidneys, remain stationary perhaps for years as they become harder. Those most frequently involved are the cervical, the axillary and the inguinal chains.

On cross section, they are quite homogeneous, glassy, pale reddish gray or slightly brown. Sometimes a granular section surface is found, at

times discernible only after the tissue is hardened. Sometimes, slight caseation is recognized microscopically; in other cases irregular macroscopic, cheesy areas, or quite coarse caseous inclusions are seen.

Microscopically, we see proliferation of spindle and large epithelioid cells in rounded or confluent clumps and strands with scattered giant cells (fig. 129d, and a larger one approximately in the center). Glassy, lumpy, or finely granular masses without nuclei denote the areas of caseation in this large cell proliferation (fig. 129c).

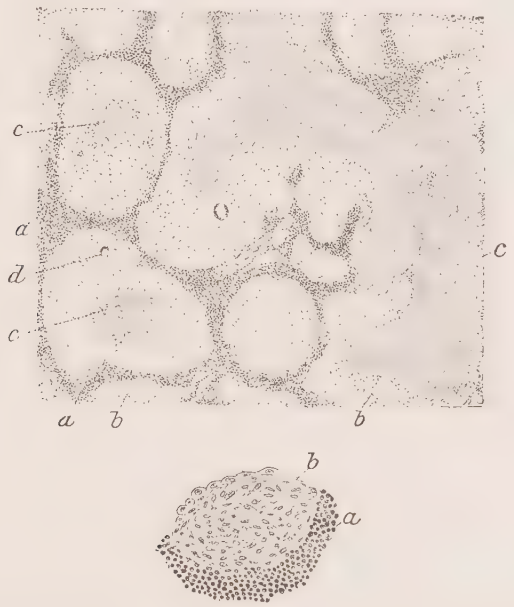



Fig. 129.—Large cell tuberculous hyperplasia of lymph node. From a hard cervical node the size of a walnut; enlarging for 10 years in a 24 year old girl, hereditarily handicapped. Cross section macroscopically almost homogeneous, glassy, light red brown. a, Very cellular lymphoid tissue, cells rounded; b, large cell tuberculous proliferation; c, caseous material; d, giant cell. Upper illustr. low power, lower high power.

The large cell proliferation (fig. 129b) stains less than the remaining lymph tissue (fig. 129a), and these rests frequently show hyalin degeneration combined with thickening of the reticulum fibres. Shiny, broad columns without nuclei between the lymphoid cell masses stain bright red (with hemalum-eosin); such an area is shown in the center of the illustration.

To demonstrate bacilli, Mathias recommends treatment of microscopic sections with antiformin, like sputum.

Sometimes caseation is more extensive, and the diffuse and chronic forms blend, but the nodes remain hard. If much connective tissue is produced, it may be spoken of as indurating tuberculous lymphadenitis (see Walz).

Since isolated, sharply circumscribed tubercles appear occasionally in this large cell, hyperplastic, tuberculous lymphadenitis, the separation between (a) and (b) is not an essential, but a formal, gradual one, according to the more or less intensive action of the tuberculous noxae, (see p. 267 under lymphogranulomatosis in reference to the peculiar form described by Sternberg).

Further changes in any tuberculous lymph nodes are secondary softening and suppuration of caseous areas. Cavities within the glands spread to a caseous purulent periadenitis perforating into a serous cavity (the pericardium etc.), the bronchi, the skin, most frequently of the neck. The perforation is through a narrow fistula or a broad, crateriform ulcer with margins lined by pale, flabby, tubercle-containing granulations. This may heal completely, spontaneously, when pus favors the elimination of the caseous material, or after surgical measures. The resulting scars are retracted and deforming, resembling those of burns.

Streptococci play an important part in suppuration of tuberculous lymph nodes (v. Brunn).

But the caseous material may calcify, as in the bronchial and mesenteric chains, etc. Some of the cheesy material may be absorbed, the remainder is thickened and hard. Most of the bacilli are destroyed; but living organisms are sometimes found in these calcified foci (lit. Wegelin). The node contains a knobby or rounded lime concretion, firmly enclosed in a connective tissue capsule. Well preserved remnants of gland tissue may still be present, or the whole gland undergoes fibro-caseous atrophy.

The cervical nodes, especially the submaxillary group, are those most frequently affected by all forms of tuberculosis. Sometimes the deep cervical nodes form knotty chains along the jugular vessels. There is a tendency to softening and rupture through the skin. The starting point varies. Sometimes there are indications of general tuberculosis, and sometimes there is tuberculosis in the neighborhood, especially in the tonsils (Hanau, Schlenker, Mitchell, lit.). Dental caries (Starck), *i.e.*, a tuberculous periodontitis (Partsch), caused by invasion of the tooth by tubercle bacilli, or tuberculous root granulomas, are also frequent (Euler, lit.). Tuberculosis of the nose, tuberculous otitis or so-called scrofulous eczema of the lips, or tuberculosis of the skin of the neck also occur. It is important to note, as Bandelier, among others, emphasizes, that the mucosa of the intact mouth cavity does not prevent invasion of lymph vessels by tubercle bacilli, (and other pathogenic organisms); thus no primary focus may be found. Indeed, Hedrin considers this the rule.

Regional lymph node tuberculosis may follow tuberculosis of the skin. According to the experiments of Babes and C. Frankel, bacilli may penetrate the skin without causing local changes; others, however, always saw

tuberculosis of the "vaccinated" area, and the regional lymph nodes under such conditions (Takeya and Dold, J. Meyer).

Bronchial nodes are involved secondary to pulmonary tuberculosis; indeed, according to Takeya, they are always tuberculous in phthisis, if not macroscopically, at least, microscopically. They may also be infected by bacilli which have passed through the lungs without leaving traces, and consequently may be primarily diseased; or they are, as assumed, infected by caries of adjacent parts (vertebral column, ribs, sternum, clavicle), or from mesenteric lymph nodes. The nodes are gathered into large caseous lumps, hard or soft, with caseous, or caseous-calcareous inclusions. Infection frequently spreads from them to the anterior mediastinal and eventually to the cervical, and to the bronchial nodes of the other side. But they are not a central organ of lymph channels, a "lymph heart" in the sense of Weleminsky (see Oehlecker and others; Sukiennikow—Topographical Anatomy). The mesenteric nodes are infected from intestinal ulcers (see there), or directly by tubercle bacilli in the chyle, as in infants drinking infected milk. Especially those in the mesentery of the ileum become massed caseous clumps, to which the ileum is closely approximated. Intestinal absorption is much disturbed and such infants usually have a distended abdomen, diarrhea, and exceedingly foul smelling stools. In spite of an insatiable appetite, they usually die of emaciation (so-called tabes mesenterica). In other cases, peritonitis follows perforation of a lymph node, sometimes of only a single caseous-calcareous node, according to Corner, in the ileocecal chain of adults, in the mesentery of the ileum of children; but, according to Thiemann, these differences do not exist. There may be no other tuberculous foci; the primary tuberculous mesenteric lymphadenitis itself may be of surgical importance (mistaken for appendicitis-Gehrts).

A generalized tuberculous lymphadenitis is encountered occasionally, but the avenue of infection is usually obscure. Big knobby growths, with tumor-like appearances, reach the size of hen's eggs, and are found everywhere (see p. 264, lit. by Garner who describes a case observed by the author in a 49 year old man; also Haerle).

If the histological examination of an excised gland leaves any doubt as to the diagnosis, the presence of tubercle bacilli can be shown by the antiformin method described by Uhlenhuth, (see Hart and O. Lessing), or by the animal test (for quicker evidence, see Esch).

It is of great practical importance to remember that tuberculosis of lymph nodes shows great variation in reference to its locality, especially if under the skin, and may cause surprise when mistaken for a true tumor. Many examples might be quoted.

As long as lymph nodes retain virulent bacilli, the entire organism is in danger of general infection.

Not infrequently a caseous lymph node is the point of origin of general miliary tuberculosis, of a more chronic general tuberculosis of the internal organs, or of a tuberculous meningitis. This is due to rupture into the venous system (see p. 159) or into a lymph trunk leading into the thoracic duct (see p. 175).

In children, caseous bronchial lymph nodes cause extensive acute caseous pneumonia, especially in the presence of a simple bronchopneumonia due to measles, scarlet fever, etc., (see under lung).

The term "scrofulous glands" is applied especially to chronic granular swellings of the neck, now known to be tuberculous, but formerly considered a special disease (older lit. by Orth). Like lupus, it is a particular form, peculiar to children, of the many disease pictures caused by tubercle bacilli. Its prognosis is relatively favorable. The clinical picture of scrofula is that of lymph gland swelling, chiefly of the cervical, bronchial and mesenteric chains. These may, however, sooner or later develop typical caseation and softening, or fibrous changes, and also true tubercles with a tendency to fungoid (tuberculous) bone and joint affections, more rarely, to tuberculous pulmonary processes. It is also spoken of as tuberculous scrofulosis. Chronic phlyctenular conjunctivitis, blepharitis, keratitis, chronic inflammations of the ear, pharynx, nose, swollen upper lips, (resemblance to a pig's snout, thus deriving the name scrofulosis, from sus scrofa), as well as the "scrofulides" presumably caused by tubercle toxins, (see skin), are all manifestations of the process.

Swelling, increased secretion of the nasal mucosa, fissures at the nares, thickening of the nose, chronic edematous excoriations of the upper lip, eczema of the swollen skin on the head and face with a tendency to ooze and to form crusts in conjunction with eye affections, produce the characteristic scrofulous facies. The external regions named are in most cases the portals of entry of the infection of the lymph nodes. In all cases of scrofulosis the cutaneous tuberculin test of v. Pirquet is positive (see Eilers). The congenital familial constitutional anomaly known as status lymphaticus (see under thymus), which is called by Czerny "exudative diathesis," is best separated from acquired lymphatism. It is a congenital inferiority, rarely absent from scrofulous children, characterized by a pasty appearance, flabby fatty tissue, tendency to persistent inflammatory reactions of the skin and mucosa on account of the increased irritability of the lymphatic apparatus, liability to infections, etc. This is the fundamental reason which, with a tuberculous infection added, leads to the scrofulous symptoms (Escherisch, Moro, Schutz, Heubner).

In reference to the importance of circular caries of the neck, see under teeth.

**Syphilis of Lymph Nodes.**—Constitutional syphilis causes two changes:

Cellular hyperplasia. The lymph nodes, rarely enlarged beyond the size of a hazel nut, mostly much less, become hard (indolent bubos), and show pale grayish red section surfaces.

This condition develops in the secondary stage not only near the original focus of infection but also elsewhere, as in the inguinal, deep cervical, brachial, etc. chains.

Microscopically, the first impression is due to the increase of lymphoid cells, but the sinus endothelium may be increased, the lattice fibres (predecessors of the colloid-producing connective tissue fibres) may be thickened and increased, (see Roessle and Yoshida), the reticulum fibres become thickened, while the trabeculae show spindle cell penetration, and the vessel walls cellular infiltrations.

Swelling and induration may recede from fatty disintegration of the cells which results from antisyphilitic therapy, and the lymph nodes may shrink to firm, fibrous nodules.

According to Fruhwald, spirochetae are often found in the regional lymph nodes, not only in the primary stage at the time of the eruption of the exanthem, but also in the later secondary stage, and even in the latent stage into the third year. In congenital lues the unchanged glands may contain spirochetae.

Formation of gummata is rare and occurs only in old gummatous lues in isolated (regional) hyperplastic lymph nodes. In a 75 year old woman with amyloidosis, the author saw gummatous lymph nodes up to the size of walnuts at the hilum of the liver, and multiple gummas of the liver itself. In two other cases, gummatous cervical lymph glands and cicatricial gummas of the neck were found.

On the section surface are yellow, dense, elastic, firm, somewhat prominent angular nodules, or connected map-like strands. The nodules have but little tendency to soften, but are dry with a fatty composition. On that account they rarely rupture, but shrink, thus differing from tuberculous caseous lymph nodes which, even if they do not break up, show small cracks on the smooth section surface.

Microscopic diagnosis and differentiation from tuberculosis may be difficult. In old cases it is impossible, as a rule, to demonstrate spirochetae. Vascular obliteration indicates luetic changes (see Fasal).

Little has been reported in reference to changes in the lymph nodes in congenital lues. In reference to the finding of spirochetae, see above (also Schlimpert). Histological changes have been found in some of the cases and consist, according to Bartel and Stein (lit.), of increase in the

endothelium and phagocytosis of lymphocytes by it, which coincided with the observed decline of lymphocytes, and an increase and greater density of connective tissue. Necroses were also seen.

3. In glanders, small cell infiltrations occur as well as hemorrhages.

In leprosy, the lymph nodes swell and contain bacilli, often in large numbers. The lymph nodes become firm and yellowish white.

**Translator's Remarks.**—Tularemia was reported in many areas of the United States up until 1926, when there were 34 states in which the disease appeared. Its identity to "Ohara's Disease" in Japan has been demonstrated. Human infection occurs mostly from wild rabbits, via the bite of the horse fly (**chrysops discalis**), the wood tick (**dermacentor andersoni stiles**) or by inoculation of the hands or conjunctival sacs by contact with the internal organs or fluids of infected rabbits, flies or ticks. A common history is that of infection of the fingers or hand occurring during skinning or dressing of wild rabbits. Clinically, two types may be differentiated: (1) the glandular, with or without an apparent primary lesion on the hand or conjunctiva, and (2) the typhoidal. The cause of the disease is the **bacterium tularense,** a small, non-motile Gram-negative rod. This grows on a complicated media, such as coagulated egg yolk or serum glucose cystin agar, and not on plain agar. Cultures can not be made direct from the patient, but only after inoculation of human material into rabbits or guinea pigs, from which the organisms can be recovered from heart's blood, liver or spleen. Spleens of infected guinea pigs remain virulent for at least a month in pure glycerin at ice box temperature, thus affording a convenient means of shipping. The blood of infected humans develops specific agglutinins after about a week and the diagnosis of the disease can be established in this way with dilutions of 1:10 to 1:160. The organisms are not stained with ordinary dyes, nor have they been demonstrated in human tissues as they have in animals.

The infection runs a much more severe and acute course in animals than in man. Tularemia should be suspected when a rabbit or guinea pig shows a spotted condition of the spleen and liver. (For details, see lit. below.) Pathologically, differentiation from tuberculosis or other granuloma is the key note. Grossly, the lymph nodes swell, become infiltrated and hard, but soon break down and disclose a cheesy, purulent necrosis. Microscopically, the first reactions are endothelial proliferation in capillaries, resulting in the accumulation of endothelial cells and giant

cells around the organisms. Mitoses are abundant in the capillary endothelium; the vessels are narrowed and obliterated with resultant necrosis. The latter calls forth polymorphonuclear leucocytes which help the later softening. Around the focus, there appears a cellular granulation tissue. Secondary necrotic (daughter) foci complete the picture, and the plump fibroblasts arranged radially increase the resemblance to tuberculosis. But no bacilli are found. Excised masses produce the disease in animals, the patient's blood serum contains specific agglutinin and the general clinical picture is quite different. For descriptions and lit., see Francis E., J. A. M. A. 84: 1243: 1925; Permar, H. H., and Weil, G. C., Am J. Path., 2: 263: 1926; Francis, E. and Callender, G. R., Arch. Path. & Lab. Med. 3: 577: 1927.

### Hyperplastic Proliferations and Tumors

**Leukemic Lymphomas. (Leukemic Adenia, Langhans).**—In the leukemias (see p. 198, under blood) with their increase of leucocytes in the

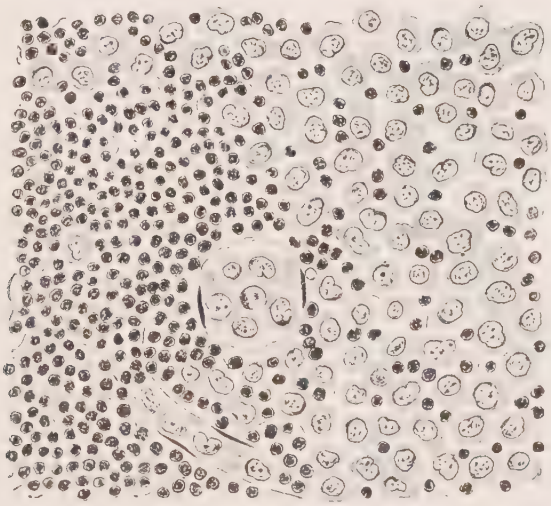


FIG. 130.—Myeloid metamorphosis of a lymph node follicle in acute myeloid leucemia. On the left remaining adenoid tissue, reticulum filled with lymphocytes, to the right myeloid cells (myeloblasts); two capillaries with myeloblasts and some erythrocytes (angular) within. Oxydase reaction positive. From the case p. 238 (high power).

blood, there is one form especially designated as lymphatic leukemia, often combined with extraordinary enlargement of the lymph nodes throughout the body, but favoring those of the neck, axilla and inguinal region. The increase of lymphocytes is thought due to increased production in these nodes.

Microscopically, there is proliferation of the lymph adenoid tissue which extends from the follicles into the interfollicular tissue until finally the

architecture is entirely wiped out, except possibly a few remains of follicles. The fibres of the reticulum are irregular, and delicate; later they are thickened, the meshes contain small lymphocytes uniform in size, with various larger cells scattered among them. The capillaries likewise are plugged with lymphocytes.

In the myeloid form also, the lymph nodes undergo a change similar, in this case, to the hyperplastic proliferation of the bone marrow, and may thus produce and distribute into the circulation, cells similar to the specific bone marrow cells (see p. 201).

The nodular enlargement is usually less marked in comparison with the lymphatic form and may be absent. The inguinal glands are much more frequently enlarged than the cervical and axillary chains.

Microscopically, the follicles remain intact at first, while the interfollicular tissue undergoes metaplasia into marrow-like substance (p. 201). The greater the extent of cellular myeloid proliferation, which begins with focal, often centrally located masses, the more the follicles disappear, but they take no active part. Finally the whole lymph node is nothing but myeloid tissue.

There are analogous changes in the spleen and bone marrow. The nodes are often enormously enlarged. Individual glands in the neck swell and neighboring glands follow. Whole chains are formed with glands reaching the size of hen's eggs or fists. Finally all the lymph nodes participate. As a rule, these lymphomas are painless, movable, and with few exceptions, unattached to each other or to the skin. Necrosis is absent.

It makes little difference where the border line of "lymphomas" is placed; the variations are merely quantitative. Microscopically the capsule is infiltrated as a rule.

Lymphomas are mostly soft, juicy, medullary, but in older cases when the reticulum is increased they are harder; the fine fibrillae become thicker, fibrous, and show some decrease of cells in their meshes. Nevertheless cellular juice can still be squeezed out.

In reference to the appearance of other leukemic foci—so-called lymphomas in other organs (liver, kidneys, lung, skin, peritoneum, dura, heart, intestines, buccal cavity, etc.), which macroscopically may resemble tubercles or tumors, see under leukemia (p. 203) and under the organs mentioned.

**Aleukemic Lymphomas.** Simple local or regional lymphomas (or lymphadenomas) consist of proliferations of lymphoid tissue and later bacony induration of tumor-like extent, which involve one or more adjoining lymph glands, usually of the neck, but occasionally in the axillary or inguinal regions, or lymphoid tissue elsewhere, such as in the palate,

lachrymal glands, salivary glands, etc., when the enlargement may be symmetrical. During proliferation the nodes are soft, but become harder as indurative changes increase; the structure is more or less preserved, or becomes indistinct just as in leukemic adeny (p. 266). The section surface may show diffuse change, or differentiation between the remaining, softer, vascular substance and the denser, somewhat glassy, pale grayish red areas, *i.e.*, foci, which project. The lymph node is movable, the growth is steady, often protracted, and no swelling and regression take place, as in inflammatory hyperplasias and sometimes in leukemias. The blood is unchanged.

The course is afebrile and benign. Nothing positive is known as to the causes. Infectious factors are suspected. In the macroscopic differential diagnosis there must be taken into consideration, leukemia, lymphogranulomatosis and the so-called large cell hyperplastic form of tuberculous lymphadenitis.

Aleukemic adeny (fig. 277) which may be called aleukemic lymphadenosis, or true pseudoleukemia, is not accompanied by leukemic blood changes but otherwise it resembles quite closely leukemic lymphadenosis. The hyperplastic, progressive swelling may pass from one node to another, macroscopically, sharply confined to the nodes, but here, as in the leukemic type, lymphatic overgrowth may occur in other organs, *i.e.*, wherever there is lymphadenoid tissue, however minute in amount. The special question is then the participation of the lymph nodes in aleukemic lymphadenosis (p. 205) with its generalized enlargement of the nodes, splenic tumor, and finally, most of the other organic changes of leukemia (lymphatic type). The blood sometimes shows an increase of lymphocytes, and the disease may actually be a prestage of true leukemia (v. Domarus, lit.). Aleukemic myelosis (p. 205), which in fact is quite rare, is not considered, since swollen lymph glands play no part. Then too, as in leukemia, there is a tendency to hemorrhages and inflammations; there are also acute forms, (see Lepehne), and according to Turk, transitions from aleukemic lymphadenosis into lymphosarcoma. But since the similarity does not extend to the blood condition, Cohnheim called this affection "pseudoleukemia" (see p. 204), a designation considered by some as out of date and needless (see Herz, Kraus). The author however, thinks it useful (see also Pinkus), and Naegeli admits that the expression "pseudoleukemia" cannot be abandoned by the clinicians (see Wulff) because there are clinical pictures which are at first a complete expression of lymphatic leukemia, *i.e.*, as long as no blood examination has been done; histological examination discloses the nature of the anatomical changes in the lymph nodes. Thus pseudoleukemia is shown to be (1) aleukemic lymphadenosis, or, aleukemic adeny, called by Pinkus "true" pseudoleukemia, or (2)

lymphogranulomatosis (see below) or, as Pappenheim calls it, granulomatous pseudoleukemia, or (3) occasionally generalized tuberculous lymphadenitis, or, much more rarely, a luetic or leprous granuloma, or what is still more rare, generalized sarcoma of lymph nodes (see there). The separation of pseudoleukemias into the histological groups 1 and 2, is considered by the author a step in the right direction to better understanding in this matter, distinguished, more than any other pathological question, by mixed terminology making unification difficult (see Pappenheim). The following names are only a few of the many older and later designations for aleukemic adeny: simple adeny (Langhans), adenia (Trousseau), Hodgkin's disease, malignant lymphoma (Billroth), aleukemic malignant lymphoma, in contradistinction to leukemic malignant lymphomas (Orth), lymphsarcoma (Virchow), and lymphomatosis (Turk), or malignant (pseudoleukemic) lymphadenomatosis (Pappenheim). In any case the term "malignant" is not advisable. It is not used for aggressive leukemic proliferations, and should be reserved for actual malignant tumors (malignant blastomas).

The lymph glands become singly diseased, or, more usually, in larger groups and chains in the cervical region, above the elbow, inguinal, popliteal, etc. They are usually not adherent to the skin, and like benign tumors, are movable over their surroundings. There is no tendency to necrotic disintegration, and, as in leukemia, swelling and regression are observed. There are cases in which the lymph nodes alone are affected. The author saw, among others, such a case in an 82 year old woman in whom the inguinal, axillary, abdominal, and tracheal lymph nodes were enlarged as single, sharply circumscribed nodes and as masses the size of a fist. There was no leukemia. The bone marrow, also involved, was grayish red, glassy, and dense. The enlargement may assume enormous proportions. Sometimes the nodules are soft, grayish red, and histologically show the peculiar characteristics of lympholeukemia except that the blood in their vessels is not leukemic. There is, nevertheless, a restriction to be made; the cells are usually not as uniform as in leukemia, but are larger; polynuclear, and isolated giant cells with many nuclei are also present. There are numerous eosinophilic cells (see Pepper, Lincoln). In sections removed for diagnosis, differentiation from round cell sarcoma may be difficult.

In other places, or in other cases, the lymph nodes are hard, whitish-red or grayish-white and resemble ordinary indurated lymph nodes histologically. Adjacent nodes do not fuse, and even when in large masses, the composition of each individual node is still recognizable.

Ghon and Roman (lit.), among others, described as a rare variation, a plasma cellular pseudoleukemia (aleukemic lymphadenosis), which they

thought related to a plasmacellular leukemia. It is questionable, however, whether there was a systemic affection (Ghon and Roman, Naegeli) or some peculiarities depending on simultaneous inflammatory processes which caused this abundance of plasma cells (Sternberg).

**Translator's Remarks.**—Under the name "follicular lymphadenopathy with splenomegaly," Symmers described an enlargement of lymph nodes due to follicular enlargement and increase in number. The disease was not fatal, and was relieved or even cured by the application of X-rays.

**Lymphogranulomatosis,** (Paltauf, Sternberg), more exactly, lymphomatosis granulomatosa, or granulomatosis textus lymphatice, is called Hodgkin's disease or malignant lymphoma by most writers (Benda). It is a frequent, chronic, infectious, inflammatory disease which attacks the lymphatic hemopoietic system which develops a special granulation tissue. Its striking similarity to the infectious granulomatous tumors (p. 255), and, on the other hand, its own peculiarity, suggest some specific cause thus far not isolated, as an etiologic factor. The first and main point of attack is, as a rule, the lymph nodes.

It is most frequent in males between 30 and 40 years of age. The blood picture is not uniform, but occasionally shows a leukocytosis and eosinophilia. In the chronic course of the disease there are intercurrent fever, loss of strength to cachexia, frequent sweats, often pruritus and diarrhoea. Its course is often accelerated by superimposed tuberculosis. Amyloidosis may appear (lit. M. Meyer; and see the observation of the author on p. 270), possibly due to toxic effects of the granuloma (Paltauf).

Macroscopic condition of the lymph nodes. The cervical chain is usually attacked first and is sometimes the only group. By degrees, others are involved in the mediastinum, axillae, inguinal region, mesentery, etc. The glands grow to the size of a fist; individual ones may reach the size of hen's eggs; at first, or always, they are movable in respect to each other, but may adhere and fuse to the adjacent tissues. They are soft or moderately indurated and of considerable size, or harder and smaller according to whether the changes are young or old. The softer glands on section are moist, grayish red to grayish yellow or grayish white, occasionally small and nodular, and, what is characteristic, although not always present, show bacony, cloudy, angular or map-like yellow foci of necrosis. The older hard ones on section are glassy, grayish white resembling fish flesh, often homogeneous; they may show necrotic inclusions or small brown spots of pigment containing iron. Macroscopically, carcinoma and leukemia must be taken into consideration in the differential diagnosis.

In the first stage, the microscopic picture is chiefly an intensive catarrh of the sinuses, or perhaps only lymphatic hyperplasia. The most striking picture is in the second stage, at which time the changes are fully developed; a peculiar granulation tissue is arranged in focal nodules which contain a remarkable variety and a lawless conglomeration of cells. There are small and large round cells (lymphocytes), many spindle shaped fibroblasts, cells of an epithelioid nature rich in protoplasm, with large oval nuclei, frequently poor in chromatin, eosinophilic leucocytes scattered diffusely or in foci, in quantities never seen in other lymph node diseases, and an abundance of the so-called Sternberg or Dorothy Reed giant cells which may be polynuclear, but which more often show a branching, antler-like or lobulated nucleus, rich in chromatin as a rule, but at times, paler, with large nucleoli, similar to megakaryocytes. These are frequently united to adjacent giant cells and reticulum fibres by protoplasmic prolongations. Plasma cells are also numerous especially in the young outer zone of the nodular foci. Since they are present in larger numbers in the early stages of the granuloma before it assumes its typical character rich in giant cells, they are plainly a proof of the inflammatory character of this new formation. In the focal necroses the former tissue elements often remain as shadows. On the other hand, there may be a tendency to fibrous, cicatricial, often hyalin, tissue formation. In the third stage, a healing process may even predominate in some areas. In small hard nodes, the cellular abundance recedes spontaneously or after x-ray treatment, as the author has seen in accordance with K. Mayer, but in isolated places characteristic cellular tissue can still be found. In the formation of this granuloma, therefore, there participate lymphocytes, endothelium of blood and lymph vessels (Sternberg) and interstitial tissue (reticulum) (see Ruffin, Hauck, etc.). The fact that this peculiar granulomatous tissue appears first as nodules, with normal lymphoid tissue in between is important in the microscopic diagnosis. Wherever the polymorpho-cellular tissue spreads, the organic structure is completely destroyed; in time the whole lymph node is involved.

Charcot-Newmann crystals appear in a few days if the glands have been preserved in fresh condition; even in this case their close relationship to eosinophiles is shown (During, lit.).

Extension occurs step by step until many parts of the system are involved (generalized granulomatous lymphomatosis), or it localizes into a circumscribed granulomatous lymphomatosis. In the generalized form, there are localizations of the process in the spleen (country sausage spleen), in the liver, in the bone marrow (see Askanazy), sometimes in the lungs, often in the bronchi and along the arteries, in the pleura, pericardium, kidneys, pancreas, breasts, ovaries, testes, etc., sometimes also

in the skin (Grosz, Kreibich, Hecht, Koenigstein, Arndt, Hirschfeld, Doesseker, lit.), usually with nodule development in the internal organs. The throat is rarely invaded (Fahr). The nodes become involved more or less generally, one group after another, or only partially, or single localized groups are attacked. Thus there are local lymph granulomas of the cervical, axillary, inguinal, or mediastinal glands. The latter when fused into masses with extensions beyond the lymph nodes give the impression of malignant tumors. In a 60 year old woman, the author saw a local lymph granuloma the size of a small fist as a conglomeration of some of the axillary glands of one side. The peripheral nodes remained intact, but there was infiltration of musculature and skin, and fungiform

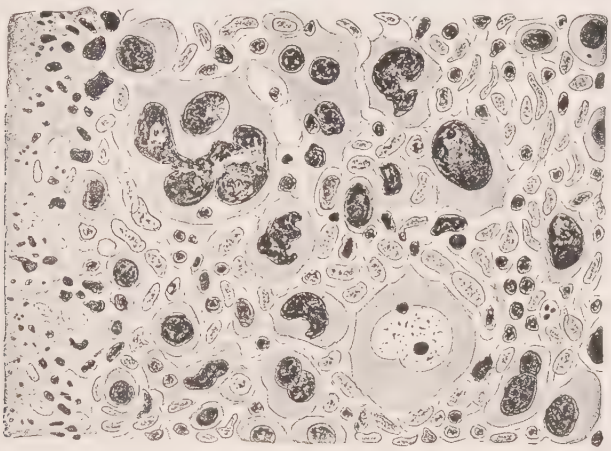


FIG. 131.—Granulomatous lymphomatosis. Polymorphous cells to the left becoming necrotic. From a man 34 years old with greatly enlarged cervical, axillary, inguinal, bronchial and abdominal lymph nodes and porphyry spleen (18:13:5). In the lung, enveloping of bronchi and vessels beginning from the hilum. Bilateral pectoral muscles and mammae filled with nodules and infiltrations. Lymph edema at anterior thoracic circumference. In some lymph nodes and in the liver typical tubercles (combination with tuberculosis) × 360.

penetration of the latter. It was supposed to have followed soon after the closure of a chronic fistula of the finger. An immense tumor in the mediastinum may invade like a malignant tumor into lungs, bronchi, vessels, even the esophagus and trachea (K. Meyer, lit.). Invasion of the musculature of the chest, the vertebrae, with compression of the spinal cord, the sternum and the skin has also been observed. Isolated tumor-like lymphgranulomas are rare in the stomach and intestines, with (Eberstaat) or without participation by lymph nodes (Schlagenhaufer, see Catsaras and Georgantas also), and are even more rare in the spleen (lit. by Naegeli).

The two following cases are characteristic examples of lymphogranulomatosis. A 52 year old woman (p.m. 599, 1906, Basle), 55 kilos body

weight, lymph nodes at hilum of right lung changed to tumor masses the size of a child's fist, consistency of a normal spleen, moist on section, grayish white, small, lobular and caseous, necrotic in areas. The individual glands were still well circumscribed. From the bifurcation upward laterally on the trachea were enlarged lymph nodes, on section grayish-white, moist, with bacony insertions projecting somewhat on the section surface. Spleen 234 gms., 15 × 8 × 3.5 cm., surface smooth; some nodules to the size of cherry pits were palpated towards its indented margin; on section somewhat glassy, transparent, and showed inclusions of tumor-like masses, round and irregular, with leaf-like contours, whitish yellow and brownish red, partly necrotic, but firm. The amyloid tests was positive as in the firm liver (2156 gms.), which, however, showed no nodules. There was also amyloid of intestines and kidneys, although there was no sign of tuberculosis. The microscopic findings (details by Bloch) corresponded perfectly to lymphogranulomatosis.

The other case (p.m. 125, 1907 Basle) occurred in a 47 year old woman. The cervical lymph nodes on the right side consisted of a mass as large as a fist, attached neither to the skin nor to each other; they were grayish white to gray red on section and showed yellowish and necrotic foci with map-like outlines. On the right side, the axillary, inguinal and iliac nodes were more or less enlarged, the first into a mass as large as a goose egg; the left chains were smaller. The spleen (1002 gms.) was slightly firmer and showed bosses and some white, translucent nodules on its surface. On section the pulp was dark red, soft, with many, very irregularly scattered, often closely grouped nodes and nodules and leaf-shaped branching infiltrations, many plainly following the follicles and branchings of the adenoid tissue. The inclusions were grayish white with caseous spots. In the liver, only isolated grayish white, rounded or angular nodules were found. There was a general anemia, high fever, no characteristic blood picture, ascites, no tuberculosis, and the microscopic findings were typical.

**Differences (*a*) and Similarities (*b*) of Lymphogranulomatosis to Malignant True Tumors.**– (*a*) When many nodules or nodes of lymphogranulomatous tissue appear in the internal organs, or in one or a group of lymph nodes, it is not as in true malignant tumors, a metastasis by transport of tumor cells into new localities and their subsequent development, but is an equivalent autochthonous tissue reaction to a certain noxa. In lymphgranulomatosis, the conditions are similar to those in which a stimulus to suitable pre-existing tissue cells causes a given granulomatous response as by tubercle bacilli or spirocheta pallida.

(*b*) On the other hand, the infiltrating and destructive growths produced by some local lymphogranulomas are very similar to those of malig-

nant tumors. But this does not necessitate the assumption of especially malignant qualities to the lymphogranuloma, *i.e.*, a sarcomatous change; for this reason, the name "malignant granuloma" (Benda) is justified only in describing its aggressive character; the same growth is occasionally seen in infectious granulomas of known etiology such as tuberculosis, *e.g.*, fungoid tuberculosis or fungoid syphilis of the testis or in the extension of a fungus to the various soft parts, etc.

**In Reference to the Name, Hodgkin's Disease.**—Etiological questions regarding lymphogranulomatosis.

The designation "Hodgkin's disease" for lymphogranuloma, again recommended by Chiari (Yamasaki), Warnecke and others, is practical on account of its brevity, but as Fabian and others have shown, it is inexact, since of the cases described by Hodgkin (1832), as far as it is possible to identify them, only a small number were actual granulomas (see Sternberg). When Cohnheim (1856) created the conception "pseudoleukemia," "Hodgkin's disease" disappeared in this collective term. Later, Paltauf, and then Sternberg (1898), recognized lymphogranulomatosis as different from other pseudoleukemias. First they called it a peculiar form of tuberculosis of the lymphatic apparatus, because Sternberg frequently found essentially analogous changes (*i.e.*, granulomatous) in cases in which tuberculosis was present elsewhere in the body, and in which typical tubercles appeared in the peculiarly changed lymph nodes, *i.e.*, nodes with Langhan's giant cells, epitheloid cells, caseation and tubercle bacilli. Paltauf then assumed it was an attenuated form of tuberculosis, but later abandoned this view in favor of an unknown etiology. The combination of lymphogranulomatosis and tuberculosis is a more or less common state of affairs (see explanation to fig. 131). Sternberg then modified his opinion, but finally believed, in view of Lichtenstein's experiments, that attenuated tuberculosis may play a part, although he acknowledged the lack of conclusive proof. Since, etiologically speaking, no other plausible findings are at hand, and since perforce the general assumption of some special inflammatory agent is accepted, (Benda), Eug. Fraenkel and Much have again brought this question to active discussion by their demonstration of granular rods, positive to antiformin, but not acid fast, and recognizable with an improved Gram stain; these organisms are considered closely related to tubercle bacilli, but not identical with Much's granula of tuberculosis.

Their findings have been verified in certain quarters including two works of Beumelburg and Kusunoki from the author's institute, but not by others, *e.g.*, Ceelen and Rabinowitsch. The opinions to date are these: most authors accept the probability of a bacillus, if not identical with the common tubercle bacillus, yet closely related; a small minority believe

they are attenuated tubercle bacilli (Lichtenstein, lit., see under tuberculous action, chapter lung) in a form, qualitatively changed (compare references by Herxheimer). It is an unsolved question made more difficult by the fact that the accidental admixture of tuberculous foci can never be absolutely eliminated in the material for cultures and animal inoculations (lit. in ref. to lymphogranulomatosis in appendix). [See J. P. Simonds, Arch. Path. Lab. Med. 1, 394, 1926. For examples of unusual cases, see Barron M., ibid., 3, 659, 1926.—*Translator.*]

**Especial Form. Plasmacellular Lymphogranulomatosis. Plasmocytoma.**—The generalized cases are counterparts of plasmacellular aleukemic lymphadenosis (see adeny, p. 265). The special cases show granulation tissue composed, almost exclusively, of plasma cells and lymphocytes, not only in numerous lymph nodes, but also, as in Maresch's case, in the liver and bone marrow. A local plasmacellular lymphogranulomatosis, so-called plasmacellular granuloma or plasmacytoma, with a tumor-like appearance, adopts its favorite site in the nasal mucosa, but, as the author saw in a 20 year old female, it may involve only the axillary lymph nodes of one side. In such a case (published by Frank and Kusunoki, lit.), the author observed a local granulomatosis of the nasopharyngeal mucosa and the cervical lymph nodes in a 44 year old man. The section surface of the hard lymph nodes was uneven, subdivided by connective tissue strands, and showed dirty gray necrotic foci (comp. cases of Schridde, v. Werth, Vogt). Plasmacytomas have been reported in the larynx, others suggest epuli (see there), in the conjunctiva (see Rund), as a tumor the size of a fist in the pleura, (see Klose). There are transitions of simple reactive infiltration (cases Hedinger, Zimmermann) to actual plasma cell granuloma, distinguished by marked independent cellular proliferation (see too Verse). Some consider the plasmacellular granuloma merely a variety of lymphocytoma (see fig. 145 p. 309).

**Chloroma.**—This is a rare systemic disease of the lympho-hemopoietic apparatus, usually of short duration, and characterized by hyperplasias of pea green color (cancer ver., Aran) of various intensities, not in all the proliferations, but enough in many to give it a peculiar appearance. It selects, although not habitually, (see below), and for a short time only, the periosteum of the calvarium of the occipital, and especially the orbital bones (Pfeiffer, Blumenthal), leading to a tumor-like deformity of the skull, sometimes with exophthalmus, etc. The periosteum is invaded from the marrow which is diffusely green in color, even if periosteal infiltration is absent (case of the author). Proliferations are often established in the loose connective tissue along the spinal column and its periosteum, the posterior side of the sternum, the costal pleura, in the lymph nodes, tonsils, thymus, the rest of the bone marrow and in the

nasal mucosa where the author saw green nodules the size of cherry pits in a 44 year old woman with myelocytic leukemic chloroma. Circumscribed tumor-like proliferations and nodules, green, and suggesting metastases, are sometimes found in many organs such as the kidneys, liver, heart, lungs, stomach, intestines, the skin and breast, even in the ovaries. The author saw a bilateral ovarian tumor the size of a walnut in a 53 year old woman with acute myeloid chloroleukemia. A "tumor-like" infiltration of neighboring tissue may start from various places, *e.g.*, from the vertebral column into the spinal canal (compression of the spinal cord, see Sauer, lit.) or from the bones of the skull to the dura. The classification of the chloroma is still a disputed question; should it be placed with lymphosarcomatosis (Paltauf, Risel, Sternberg, Meixner), with leukosarcomatosis, or with leukemia? Older authors (v. Recklinghausen, Dock), and many younger observers emphatically advocate from clinical, hematological and anatomical view points, (see Pauliczek-Wutscher), that the chloroma be classed with the leukemias.

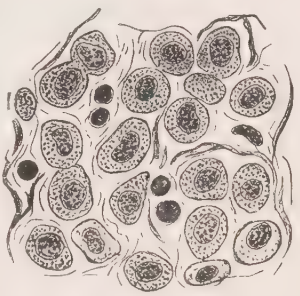


Fig. 132.—Myeloid Chloroma. Lymph nodule, almost all cells of myelocytic character with eosinophilic granules; case mentioned in text; × 360.

Tumor-like pictures and apparent metastases, especially in the acute forms, are familiar in leukemia. Leucosarcomatosis, a term we do not accept (p. 203), would also be included here. Lymphosarcomatosis is not included, since a myeloid chloroma occurs, but myeloid tissue is foreign to lymphosarcoma, and according to our interpretation, chloromyelosarcomatosis is included in acute myeloid leukemia. There are chloromas confined to the bone marrow and lymph nodes without tumor-like growth (Lehndorff, lit.). The differences between leukemia and chloroma disappear even if cases of chronic myeloid leukemia developing a chloroma with locally aggressive growth, are taken into consideration (lit. Herz). The green color is accidental, and only partially developed in most chloromas; on the other hand, it is found also in ordinary leukemias and even in chronic tuberculous lymphadenitis (v. Hansemann). Even the characteristic periosteal proliferations, especially of the skull, are not uniformly present in chloroma (60 times in 96 cases, see Kchinowloguer); they are generally absent in ordinary leukemia, but may be present in this disease (lit. by Herz). Thus chloroma is deprived of an independent position. The question which remains is whether chloroma belongs to leukemia, an opinion shared by the author, or to the tumors. Askanazy recently declared himself in favor of a separation of chloromas as malignant tumors, from "myeloid leukemia with green tumors," because macroscopic tumor

thrombi were found in the veins in at least 5% of chloromas. It must be remembered that some authors, especially Banti, have demonstrated constant microscopic invasion of the veins by leukemic proliferations in leukemia (see p. 205); these are probably only differences of degree.

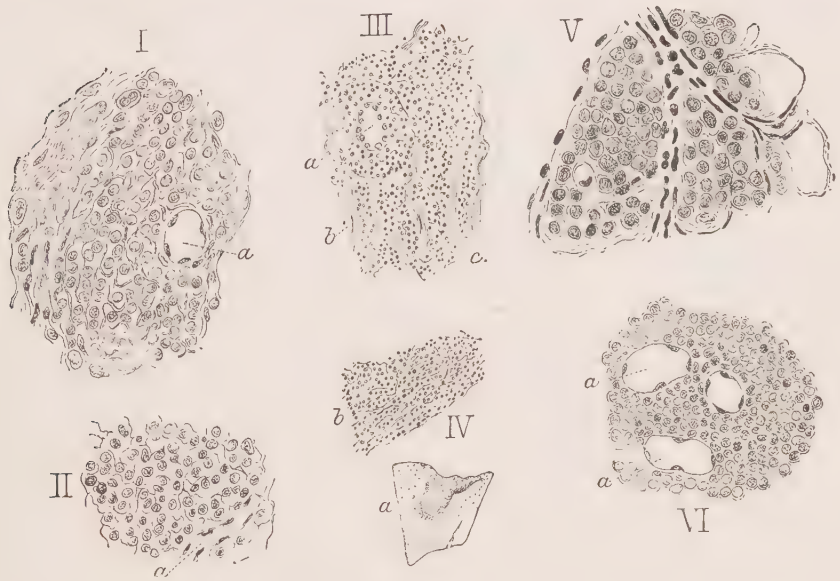
There are two forms of chloroma designated as lymphatic (most frequently, large cell), and myeloid, the more frequent. Others speak of lymphatic and myeloid chloroleukemia (Naegeli and others) or of chlorolymphadenosis or chloromyelosis (lit. by Weinberger, Port and Schutz, and especially Fabian; see also Wetter, Lehndorff and lit. in appendix). Myeloblasts are found more frequently than myelocytes, but the latter were seen by the author in the case mentioned on p. 273 in a 44 year old female. The author, among others, observed that many myelocytes, especially in the lymph nodes, are distinguished by eosinophilic granulations (see also the case of Dock and Warthin, see fig. 132). This case was a 23 year old man with a severe anemia closely akin, from the blood picture, to pernicious anemia. The lymph nodes surrounding the aorta were light green. The periosteum of the sternum showed coin-shaped green plaques, continuing slightly into the bone. There were small nodules in the kidneys. The lymph glands in the hilum of the lung were enlarged, and from there sheath-like infiltrations followed the vessels into the lung. The inguinal glands were enlarged and pale green in color. The spleen weighed 276 gms. Chloroma is relatively frequent in children and young individuals. It is finally fatal because of pressure on vital organs (Gumbel, lit.), or subsequent to an incurable systemic disease (see Fabian, lit.).

The green color, an accidental symptom (see above), may, as Beitzke remarks, be absent in a mass excised during life, while at autopsy it is present. Some consider the coloring matter a granular fat pigment belonging to the lipochromes (Huber, Chiari, Horing), while others consider it a "parenchyma" color (Virchow, v. Recklinghausen). Askanazy considers it a "pus" pigment; Pauliczek and Wutscher think it is related to myeloblasts (see Ernst). When exposed to the air, it soon becomes dirty gray, but treating with ammonia restores it (Paviot). It is preserved in Pick's solution.

**Lymphosarcoma.** Lymphosarcoma is an aleukemic malignant proliferation of lymphatic tissue imitating lymphoid tissue in more or less imperfect (atypical) manner. In many respects, lymphosarcoma, as a systemic disease of the lympho-hemopoietic system, is clearly separated from the large group of sarcomas, as we shall find later.

Kunrath early discarded the idea of actual tumor, assuming that it is a vegetative disturbance of the lymphatic system. Paltauf avoids the word "tumor," and speaks of atypical proliferation and aleukemic

malignant hyperplasia of lymphoid tissue. On the other hand, Ghon and Roman believe it has a true tumor nature, using the name "lymph adenoid sarcoma." The author rejects this opinion, and believes that lymphosarcoma is more closely related to the aleukemic lymphomas than to true sarcomas; Pappenheim considers it a special variation (Turk, Eug. Fraenkel, opposing Sternberg, Naegeli). For this reason, it is not correct to identify lymphosarcoma with small round cell sarcoma as is frequently done. The histological picture of lymphosarcoma with its greater polymorphy of cells and the essential participation of the reticu-




FIGS. 133–138.—I. From a hard mediastinal lymphosarcoma; 26 year old man, text p 278; a, capillary, to right, loose adenoid tissue; to left, interstitial substance predominates (high power). II. From a primary lymphosarcoma of small bowel of man 25, text p. 279; a, capillary (somewhat lower power). III. From a lymphosarcoma of ileum of man 74 years old; multiple primary lymphosarcoma of ileum, text p. 279. Sect. from muscularis; a, vessel with lymphoid wall; b, smooth muscle penetrated by (c) tumor tissue (medium magn.). IV. Renal metastasis from the lymphosarcoma mentioned under II; text p. 279. a, Cross section through tumor-infarct ($\frac{9}{10}$ nat. size); superficial depression, the corresponding kidney tissue is atrophic and has undergone more or less fibrous change; invading lymphosarcoma tissue. b, Taken from the parts of the apex of the cone which shows delicate lymphoid tissue (low power). V. From a large (alveolar) round cell sarcoma, quickly growing, very large tumor in a few months, occupying one side of the neck of younger man. The septa which divide the round cell complexes are vessels and fiber strands derived from them (high power). VI. From a small round cell sarcoma, infiltrating one side of the neck and the pharynx of youthful individual. a, Capillaries; small round cells lie in interstitial tissue which is without reticulum (high power).

lum, often distinguished by a tendency to fibrous thickening, is plainly different from the always soft, cellular, small round cell sarcoma, with its tendency to disintegration, and variation of the reticulum, mostly as a recession into insignificance.

It must also be stated that the starting point of lymphosarcoma is adenoid tissue of any locality, from lymph nodes (most unfavorable prognosis) to that of the pharynx, tonsils, stomach, bowel, testes, etc. More or less of the lymphatic system may participate in the proliferation, but in contradistinction to other lymphatic diseases (leukemia, aleukemia), there is never a universal involvement, nor is there typical participation of spleen and liver as in those diseases. A pronounced generalized involvement of lymph nodes, therefore, never occurs, with rare exceptions, and is an important and usually decisive difference from lymphatic leukemia and aleukemic adeny.

The following observations concern lymphosarcoma in general. The proliferation at the original location penetrates and infiltrates the vicinity but preserves its adenoid character. Its relatively aggressive tendencies are often discussed. An ordinary sarcoma as a rule shows eroding, tissue destroying properties (see p. 276).

If a lymph node is the starting point, the proliferation penetrates the capsule, invades the adjacent nodes, enters the skin and becomes firmly ingrown into a connected adherent tumor. In aleukemic adenia the lymph nodes are movable as a rule. The tumor grows rapidly, returns after operative removal, forms metastases and is highly malignant (Kundrat, comp. Exner).

The mooted question of true metastases is still unanswered, *i.e.*, transplantations from the primary tumor, or, as in leukemia and aleukemic adenia, merely equivalent similar effects of a given cause in different localities (see Pappenheim, Fabian). Paltauf speaks of the "placing of metastases," and Kundrat recognizes that metastases may reach distant organs through the blood stream.

The tumor may disintegrate, ulcerate, or may shrink in part. In aleukemic adeny there is little tendency to disintegration. Frequently, although not exclusively, young healthy men are affected more often than women.

**Microscopic and Macroscopic Appearances of Lymphosarcomatous Tissue.**—The proliferations in lymphosarcoma and in aleukemic adeny resemble more or less closely the structure of lymphoid tissue, (see p. 275, illustr. I to IV), but in lymphosarcoma an atypical architecture appears as the free cells increase in number, vary in size, and as different stages add to the irregularity of arrangement (coarser meshes) and to the thickness of the reticulum (Kundrat and Paltauf).

There are not many capillaries and larger vessels, the walls of which are always in close contact with the reticulum fibres in typical lymphoid tissue. But the chief difference is the unlimited growth of lymphosarcoma clearly seen in good paraffin sections. In preparations made by shaking, the adenoid character in relation to the reticulum is easily observed.

In young tissue, the section surface is homogeneous, pale whitish red, moist, and of soft consistency. The microscope reveals a vascular, delicate, coarse meshed, fibro-cellular network, in which the predominant cells are small and round, resembling lymphocytes (see p. 275, illustr. II, III, IV). This network may become cellular and fibrous, while the cells within the meshes grow larger, and contain several or many nuclei, (giant cells), (p. 275, illustr. I left side of preparation). This tissue is hard, less moist, paler, with macroscopically visible fibrous strands on cross section resembling fibromyomas. It can be recognized that the harder areas are the older; where the tumor progresses, it is softer (p. 275, illustr. I). These transitions from soft to hard show that it is impossible to make a clear-cut distinction between soft and hard lymphosarcomas (see also F. Muller).

**Microscopic Diagnosis of Lymphosarcoma.**—Aleukemic lymphoma is differentiated from lymphosarcoma by the more atypical structure of the latter. This atypical condition prohibits the name lymphocytoma which may be prompted by deceptive areas containing lymphocyte-like small round cells. In some cases the mononuclear round cells of lymphosarcoma are in the majority. They are larger and their nuclei almost completely fill the cell and stain less deeply than small lymphocytes. Eosinophilic cells and plasma cells without germinal centers appear, also polynuclear cells and occasional giant cells. Later reports by Ghon and Roman indicate that every cellular element of lymphoid tissue may be present. These mixed cells lie in a sort of irregular reticulum formed in the younger areas by fine connective tissue fibrillae and in older places by dense connective tissue.

It is often impossible to demonstrate malignancy from the lymphosarcoma tissue alone; the clinical course and the situation from which the specimen is derived, must be known; in other words, topographical orientation is necessary to determine whether there is an hyperplastic or an heteroplastic proliferation, *i.e.*, invasion, present. In the latter event, *e.g.*, if the preparation is voluntary muscle containing tumor tissue of more or less modified adenoid character, or, if this tissue is found in the intestinal muscularis, the diagnosis of lymphosarcoma is easy as in fig. III p. 275.

Erosive destruction of infiltrated tissue, as in the penetration of muscle fibres by ordinary sarcomas, is absent in lymphosarcoma; in fact, as in leukemic infiltration, the tissue undergoes pressure atrophy.

Hematological examinations are negative; the blood findings are normal in typical lymphosarcomatosis, or at most, show minor changes (increase or decrease of lymphocytes, see Sternberg, Weinberger, Fabian, Kreibich, M. Sternberg, Naegeli).

According to the course of the disease, two groups are differentiated, but with graduated and non-essential differences.

**Regional Local Lymphosarcoma.**- The tumor springs from adenoid tissue in some situation, grows into the vicinity, but remains in its determined region. The source is usually a lymph node.

Examples of this kind are offered by the lymphosarcomas of the mediastinum, (usually anterior). Springing from the lymph nodes or more rarely from the thymus, they develop into enormous tumors in a short time, sometimes adherent to the sternum, surrounding the vessels (veins), or organs (bronchi trachea, esophageal stenosis, pericardium, heart, pleura), and the neighboring lymph nodes (cervical), occasionally infiltrating the muscles of the neck, spinal column and sternum. Lymphosarcomas from lymph nodes are often nodular, while those starting from lymphoid tissue of the thymus (see there) develop homogeneous tissue complexes. Thus the author saw a mediastinal lymphosarcoma almost as large as a man's head, moderately firm and homogeneous, which had developed within three months in a 21 year old soldier who died of asphyxia due to tracheal compression. In the case, illustrated on p. 275 of a young man 26 years old, the nodular mediastinal tumor following the lymph channels had infiltrated the bronchi, which became stenosed, and the lungs themselves. The narrow bronchi contained tenacious mucus with great numbers of asthma spirals. The tumor masses in the walls showed beautiful lymphadenoid structure.

Sometimes distant metastases, occasionally as diffuse infiltrations of kidneys, pancreas, ovaries, etc., occur from mediastinal lymphosarcomas.

Lymphosarcoma of the mesentery sometimes remains regional, (extending only to the intestinal serosa), as does lymphosarcoma of the larynx or of one testis. In a 40 year old woman, the author saw both an immense mediastinal lymphosarcoma infiltrating the lung and heart, and a mesenteric lymphosarcoma the size of a child's head, both showing cicatricial changes, and without doubt, independent growths.

Regional localization in the neck, frequently on one side only, is also quite common. The starting point can sometimes be shown as an entire chain of nodes simultaneously diseased. They adhere to each other and to the vicinity and invade the adjacent tissue with thickening of half of the neck or all of it. Within a few months an almost monstrous thickening may be produced. In other cases the follicles of the pharynx or the retroperitoneal lymph nodes are the starting point. The nodes may swell to enormous tumors and by infiltrating the intestinal serosa, cause narrowing of the lumen.

They may also start from the lymphoid tissue of the gastric or intestinal mucosa. The preparation on p. 275, illustr. III, comes from a man

74 years old, in whom several constricting, infiltrating tumors were found in the intestines in which layers were unrecognizable, but there was no stenosis. In this case, no participation had occurred of the abdominal lymph nodes and no generalization.

The so-called endemic "lung carcinoma" of Schneeberg proved in some cases to be lymphosarcoma (lit. Fabian). The small amount of material does not permit us to judge whether this is the rule (comp. Uhlig, and see under lung).

**Generalized Lymphosarcoma (Lymphosarcomatosis).**—A general extension with metastases throughout the body, including the skin, is rare in comparison to the regional form.

Extension is rarely as general as in leukemia. As an example of this type, the following may be quoted: a machine polisher, 25 years old, sturdily built; starting point in the upper part of the ileum (see p. 275); infiltration of the bowel for 6 inches in length, causing some stenosis; icterus from narrowing of the papilla of Vater. Innumerable soft nodules appeared, both in the subcutaneous and cutaneous tissues and projected several centimeters with indentations from central fatty degeneration. Many nodules, free from disintegration, showed a whitish red, homogeneous, glassy section surface. The disintegration was possibly due in part to treatment with arsenic, which may have also contributed to the advanced fatty degeneration of the cardiac muscle. But disintegration within the nodules may occur without arsenic. In addition, flat, board-like hard, infiltrations of the pericardium nodules in the lungs, bone marrow and pleura were found. None were discovered in the spleen or liver. The symmetrical change of the kidneys was especially interesting (p. 275, illustr. IV); each showed about 20 surface indentations approximately wedge-shaped on cross section (see p. 275, fig. IVa), consisting of cicatricial tissue, containing atrophic glomeruli in the uppermost layers, but otherwise composed of clear cut adenoid tissue (p. 275, IVb).

**Difference between Lymphosarcomas and Other Sarcomas.**—(1) See p. 274 and 276 in reference to the relative aggressive character of the progressive lymphosarcoma invading adjacent tissues, compared to the destructive common sarcoma.

2. The primary tumor of lymphosarcoma, as well as its metastases, is pronouncedly infiltrating; local, as well as general extension, occurs almost exclusively by way of the lymph channels and tissue clefts either with or against the current. But, according to Kundrat, metastases may finally be spread by way of the blood stream (see also Ghon and Roman). In the case of lymphosarcomatosis mentioned above, this can easily be believed on account of the numerous cutaneous and subcutaneous nodules.

The above mentioned case (p. 278) of mediastinal tumor is an example in which the bronchial walls were infiltrated over long stretches. The case of generalized lymphosarcomatosis in which pericardium and pleura showed diffuse infiltration illustrates the same point. Of especial interest are the findings in the lymphosarcoma of the intestinal wall, illustrated p. 275 fig. III. The infiltrative character shows beautifully in the clefts of vessel walls which were practically transformed into a covering of lymphoid tissue (p. 275 fig. IIIa). In contradistinction, true sarcomas usually form knotty metastases, occasionally diffuse infiltrations, and the rare exceptions, generalized lymph node tumors, (p. 281). They prefer the blood stream for further spread. As Kundrat has emphasized, the selective choice of metastases of lymphosarcomas for certain organs such as the mucosa of the intestinal tract with its abundant lymphatic tissue is remarkable since these are rarely involved in ordinary sarcomas or carcinomas. This must be kept in mind in interpreting the point of origin of some cases. In the following case from Basle, a 54 year old woman with perforative peritonitis, there were 3 liters of fecal exudate in the abdomen, and rupture of the ileum which was diffusely infiltrated and enlarged for 12 cm. of its length; there was an immense mass of fused mesenteric lymph nodes practically unrecognizable from mesenteric tissue; bacony, whitish red tumor masses extended into the pelvis, the ovaries, the peritoneum, the sigmoid. They also accompanied the vessels as a thick coating, extending by continuity over about half of the right kidney. There were other infiltrations of the peritoneum, especially in the epiploic appendices. It was tempting to speak of primary lymphosarcoma of the intestine, but the complete picture makes it evident that the mesenteric gland tumor was the center and starting point of the process.

3. Sometimes in lymphosarcomas, the primary tumors develop in quite different regions, as in the 40 year old woman mentioned on p. 278 with tumors in the mediastinum and mesentery,—or in different parts of one region (multiple primary lymphosarcomas).

The latter process is illustrated by simultaneous involvement of several adjacent cervical lymph nodes or intestinal follicles. The illustration III, p. 275, shows a case of multiple primary lymphosarcoma of the ileum. In true sarcomas, with the exception of skin sarcomatosis, this never occurs.

4. The tendency to macroscopic disintegration in lymphosarcoma is exceptional, in contradistinction to that in the ordinary, especially round cell, sarcoma. Numerous small necrotic areas are scattered in larger tumor masses. Erosion of blood vessels is foreign to typical lymphosarcoma.

5. Isolated observations indicate the possibility of spontaneous regression of lymphosarcoma (see lit. by Exner), a process unknown in round

cell sarcoma. Macroscopically, true sarcomas, especially of the neck, frequently resemble lymphosarcoma, and their starting point may remain obscure, (lymph node, vessel sheaths, etc.). The illustrations V and VI, p. 275, present true sarcomas in youth; in one case, fig. V, one half of the neck was involved, while in the other case, fig. VI, the pharynx was also infiltrated, making it impossible to recognize normal structures. Both tumors grew quite rapidly. The first tumor was a large cell sarcoma, the second a small round cell sarcoma. Microscopically, diagnostic difficulties may arise in the harder (older) areas of the tumor. At times, the adenoid character is unrecognizable, especially if the sections are too thick. Then it may be confused with fibrosarcoma, or even carcinoma. Very thin sections prevent such mistakes, and also confusion with large cell sarcomas, in which the reticular scaffolding is partly or completely absent, (fig. VI p. 275); for the absence of erosive destruction, see p. 276.

In reference to leukemia and aleukemic adeny, it must be emphasized that the characteristic diffuse infiltrations of the liver and spleen so prevalent in these processes, are absent in lymphosarcoma. On the contrary, if complications are absent, these organs, as a rule, are rather small (lit. of lymphosarcoma in appendix).

**Sarcomas.**—Primary sarcomas of lymph nodes are rare and must be sharply separated from lymphosarcomas; they are especially different in relation to their metastases (by the blood route, without involvement of adjacent lymph nodes). A single lymph node is always the starting point of the tumor which promptly ruptures through the capsule and invades the vicinity. Primary generalized sarcomas of the lymph nodes are very rare (spindle cell sarcoma-Baumgarten, polymorphocellular sarcoma of lymph nodes and intestines—Spieler, lit., see p. 282).

The forms taken are fibrosarcoma, spindle cell sarcoma, large and polymorphocellular sarcoma, pigment sarcoma, (especially malignant and often alveolar in structure), angiosarcoma and round cell sarcoma, which is most difficult to differentiate from a soft lymphosarcoma, but thin sections with van Gieson's stain help.

Alveolar endotheliomas (quite rare) may give rise to difficulties, because they resemble carcinoma; there is always a tendency to suspect an occult primary carcinoma, rather than a primary endothelial lymph gland tumor. The author saw one, the size of a small fist, existing for 9 months in the left axilla of a 67 year old woman. It consisted of alveoli of large, angular, often vacuolated, closely packed cells with their nuclei poorly stained. The knobby tumor was closely attached to the axillary and subclavian vein and still showed lymph gland structure in some areas. Death occurred 9 days after operation; no other tumor could be found. Zahn describes such a tumor as an "alveolar epithelioid sarcoma." The

tumors described as so-called primary carcinomas (Colrat and Lepine) are probably of this variety. Von Recklinghausen and Gallina (multiple endothelioma of lymph gland and lymph channels) described such cases (formerly called endothelial carcinoma) starting from the endothelium of intraglandular lymph channels, (see Banti, Ciaccio, Ewing, da Gradi, and de Amicis, primary generalized tumor formation, lit.).

Secondary sarcomas in the lymph nodes, especially small round cell sarcomas and melanotic sarcomas, appear more frequently in certain forms. Endotheliomas, *e.g.*, of serous membranes (see under pleura), and of other localities, may metastasize to lymph nodes.

FIG. 139.—Appearance of the patient fifteen years after his first complaints which were of enlargement of the cervical lymph nodes on both sides. Excision at that time revealed myxomatous tissue. These growths have slowly enlarged and at the present time he has nodules in his axillae, in his groin and under the skin in many areas of the body. See for example above the elbow in his left arm and above his left wrist. Repeated biopsies revealed nothing but myxomatous tissue. The diagnosis of myxo-sarcoma is made but it has nothing in common with the ordinary myxo-sarcomas as met under ordinary circumstances. It seems to be a very slowly growing replacement of lymphadenoid tissue by myxomatous tissue without definite malignant properties. Age now, 32. L. H.

In certain sarcomas of bone, the regional lymph nodes are sometimes involved.

**Carcinomas.**—Carcinoma in all of its varieties, occurs only as a secondary growth. In contradistinction to sarcoma, carcinoma preferably infiltrates the nearest regional lymph nodes (the expression is used "to infect"), and further metastases may occur from this station.

Cells from the primary tumor float down the stream, or, by continuous growth within lymph vessels, reach first the cortical peripheral sinus,

but they may grow against a weak current. The cells are lodged in the reticulum, and multiply by division without respect for the structure or boundary of the lymph nodes. The parenchyma is infiltrated and destroyed, while parts of the connective tissue scaffolding and blood vessels are utilized to form septa (alveoli) for carcinoma plugs (parenchyma) and for nourishment (fig. 140), until the structure of the lymph node is completely lost. The capsule is then perforated and growth proceeds into the vicinity. In an observation by the author a remarkably late carcinomatous metastasis of the axillary glands was seen 6 years after amputation of the breast. The lymph nodes were but slightly enlarged. Hypothet-

FIG. 140.—Metastasis of an adenocarcinoma in the marginal sinus and cortex of a lymph node in carcinoma of the stomach; between the pseudo-glands is secretion; × 60.

ically, it is assumed in such so-called "late metastasis," that the body is able to inhibit the growth of the disseminated tumor elements after the primary tumor is removed (see Konjetzny, lit.).

The enlargement of the nodes may be quite considerable at times, and not at all comparable to the size of the primary tumor (see cases under esophagus).

The section surface of the purely carcinomatous lymph node is white. The consistency is hard, rarely gritty from calcification, or soft and pultaceous if the cells undergo fatty degeneration. In hard lymph nodes, the original structure is completely lost to make room for scirrhous carcinoma tissue. Manifestly, in certain cases, the tumor has marked ability to stimulate fibroblastic reaction (see Lungsgaard). They, of course,

suppurate if infected by pyogenic organisms and leucocytes invade the septa and the parenchyma.

Occasionally, microscopic investigation of regional lymph nodes demonstrates more easily the character of the primary tumor than the examination of the tumor itself. This is not rare in some hard, stenosing, carcinomas of the pylorus, in which the lymph node metastasis is often more cellular than the primary tumor. But generally, the histological character of the metastases corresponds fairly well to that of the primary tumor, and consequently shows the various forms of carcinoma. In reference to this question, see under stomach, ovaries, breast, skin, and other partly epithelial organs.

Often, it is by no means easy to differentiate microscopically between early carcinomatous infiltration and inflammatory changes, *e.g.*, in breast carcinomas in which the axillary lymph nodes show considerable enlargement and nodular changes in form. It is especially difficult to differentiate the proliferated, swollen and desquamated cells of the sinus (catarrh of the sinus) from carcinoma cells, washed in and filling the sinus (see Ewing). Necrotic changes following occlusion of lymph vessels sometimes complicate the picture (Sgambati). Gland-like structures evolving from endothelial proliferation in inflamed lymph nodes, can be mistaken for cylindrical cell carcinoma tubes (comp. carcinoma uteri). It may help to remember that carcinoma cells form connected masses or gland-like figures, usually with better nuclear staining and much more polymorphous characteristics. For so-called benign gland metastases in lymph nodes, see Dawidowsky. The papillary cyst adenomas of H. Albrecht and Arzt are of quite different type, and according to these authors, are derived from aberrant germ cells of the parotid gland enclosed in lymph nodes. They are papillary adenomatous epithelial structures in which the whole stroma is composed of lymphoid tissue. Glass (lit.) called such a tumor of the parotid region, a "branchiogenic papillary cyst adeno-lymphoma." See also branchioma of the parotid region by Ssobelew. The author saw a tumor in the parotid region, analogous to the latter, *i.e.*, a lobulated cystic tumor the size of a chestnut which, like a sarcoma phyllodes of the breast, perforated the skin.

Occasionally carcinoma and tuberculosis are combined (lit. by Krische).

### Regressive Conditions

**1. Simple Atrophy. Lipomatosis.**—As a rule, the lymphoid cells begin to disappear in advanced age, and fatty tissue enters from the hilum to displace the disappearing and hemispherically flattened lymph node. Lipomatous atrophy is sometimes found in high grade obesity and

where the atrophic nodes are enveloped by fat (for instance the mesenterics).

2. **Fatty degeneration** chiefly involves the lymphoid cells, *e.g.*, during regression of indurated buboes or non-specific inflammatory hyperplasias.

3. **Amyloid degeneration** is one of the symptoms of general amyloidosis, or is independent as in aleukemic leukemia. The connective tissue of the follicles, capillaries and arterial walls undergoes glassy changes. The reticulum fibres swell, become lumpy, displace the cells situated in its meshes, and press the meshes of the reticulum into narrow clefts (fig. 122, p. 244). The follicles usually contain smaller central amyloid foci (see Noltein, lit.). If the change is well advanced, the glands become firm, glassy, bacony, and turn brown on the addition of iodine solution.

4. **Hyalin degeneration** affects all cells, inclusive of the reticulum and vessels; they swell and obscure the architecture. If sections are stained with hemalum and eosin, the hyalin areas are bright red.

Hyalin degeneration is frequent, not only in tuberculous, (fig. 129), but also in carcinomatous lymph nodes.

5. **Calcification.**—Diffuse calcification occurs in caseous nodes, or in those undergoing other necrosis or fatty degeneration, and in dried or suppurated parts. In the latter, granular, laminated chalk concretions are sometimes found; foreign body giant cells may accumulate around them. The lymph nodes may be quite gritty and at times stony hard in psammoma carcinomas. In a large pelvic fibrosarcoma, Plen saw local "calcification metastases" in the lymph nodes.

6. **Ossification** following calcified tuberculosis is not rare, and mostly a form of metaplasia (see Lubarsch).

### Regenerative Processes—New Tissue Formation

New formation of lymph nodes may take place in post embryonal life, from embryonal rests, by division of existing lymph nodes, or by new formation within fatty tissue, particularly around tuberculous and hyperplastic nodes, or, more rarely, carcinomatous or sarcomatous nodes (de Groot, lit.; see Ritter). Lymphoid nodules (follicles with germinal centres) are often found in the gastric mucosa in chronic inflammations, or in the endometrium, tubes, gall bladder, etc., (see under thyroid and bone marrow).

**Parasites.**—Echinococcus multilocularis (see under liver) occurs in rare cases, usually with echinococcus of the liver (Morin, Pichler, Melnikow-Raswedenkow). Cysticercus is very rare. Fiedler found cysticercus cysts in mesenteric glands. Trichinae have been found in mesenteric lymph nodes (see under muscles).

## BONE MARROW

The conditions under discussion are general diseases of the bone marrow which occur partly because of its place in the hemopoietic apparatus as a blood-making organ, and partly because it is involved in certain general infectious diseases.

For special diseases of the bone marrow of individual bones, and for tumors of the marrow, see under "Bones."

**The Bone Marrow in General.**— Bone marrow has many physiological duties. 1. It is the most important organ of post natal hemopoiesis, normally supplying the adult with his erythrocytes and leucocytes. 2. Certain cells of the bone marrow, osteoblasts, or better, osteoplasts, are capable of forming bone. 3. Absorption of bone is done by osteoclasts—large polynuclear cells (absorption giant cells). 4. Megalokaryocytes are the source of blood platelets. For incorporation of the capillary endothelium of the blood marrow with the reticulo-endothelial apparatus, see p. 219. In reference to phagocytosis, *i.e.*, of pigments, by capillary endothelium (in rabbits) and of bacteria by reticulum endothelium (in dogs), see Brass (lit.).

In the vascular bone marrow are found the true bone marrow giant cells (myeloplaxes, megakaryocytes) with lobulated or ring-shaped nuclei; they have no relation to bone absorption. They are thought to be the source of blood platelets (p. 186), because increase of the latter often coincides with their abundance in the bone marrow. Their origin is disputed (primary wandering cells of Saxer?, Schridde, lit.). According to Naegeli, they are derived from myeloblasts (see p. 195), and in febrile diseases often wander into the blood during the agony, (see under lung, cell embolism). According to Naegeli and Oelhafen, they appear in the blood in every myelosis, and according to Klein, some pass into the blood normally. They may phagocyte leucocytes and erythrocytes (see Reitano).

The younger the individual, the more numerous the myeloblasts (Naegeli, see p. 195). Later, the myelocytes of Ehrlich appear in numbers. They are mononuclear cells with different granulations, among which those of the neutrophilic type outnumber the others, being the chief white blood cells in the marrow of the adult; those with eosinophilic granules are more numerous in children. Basophilic myelocytes are never numerous. The leucocytes, mostly neutrophilic, are a progressive developmental stage of similarly granular myelocytes. They enter the blood stream and constitute about 70% to 80% of white blood cells. Pus cells are derived from the bone marrow, and, in addition to mature neutrophilic leucocytes, are also composed of immature marrow cells. Red blood cells, with and without nuclei, are also found. The former are

called normoblasts or megaloblasts (p. 188) and are considered the mother cells (erythroblasts) of the non-nucleated cells. They multiply in the bone marrow by mitosis, and normally enter the blood as erythrocytes after the disappearance of their nuclei. In the newborn, normoblasts are still numerous (as to their appearance in pernicious anemia, see p. 191).

There are lymphocytes and occasional plasma cells isolated around vessels as elsewhere in the body. These are not true parenchyma cells of the marrow, and are usually sparse. In the otherwise normal red marrow of the hollow bones of children, Oehme found them especially frequent in rickets along with lymph follicles and germinal centres, and germinal foci of small lymphocytes, the source of which may possibly be traced to normal adventitial lymphatic cells of the marrow vessels (see also Hedinger). Askanazy and v. Fischer (lit.) found so-called lymph nodules quite frequently in bone marrow especially in that of older individuals. They are rounded collections of lymphocytes without germinal centres, localized around arterial capillaries. Their purpose is disputed; the discoverers think they are somewhat variable normal constituents of bone marrow; Schridde considers them pathological. The marrow contains numerous vessels with thin walls, which form a closed network created by sudden branchings of arteries joined to wide, valveless veins. The cells from the bone marrow enter the veins and there change into the final blood elements (see Naegeli).

Since these vessels are suspended in the rigid bone by means of a delicate network of branching cells, they remain wide open, gaping, and are not collapsible. The larger blood vessels, lymph vessels and nerves are located in the centre of the marrow column (details by Carnegie-Dickson).

Differentiation is made into (*a*) red marrow, formerly also called lymphoid marrow, which occurs in youthful, growing bones and is especially rich in myeloblasts, later myelocytes (see above). It is therefore also called myeloid marrow, but contains nucleated erythrocytes. It soon becomes paler, of the color of wine dregs and is displaced by fatty tissue with the exception of a peripheral zone which is (*b*) fatty marrow (yellow marrow), poor in cells. Fatty tissue is physiologically a prominent constituent of the marrow, and develops from the stellate connective tissue cells, which form the main body of embryonal marrow. Later, after birth, the connective tissue reticulum cells change into fat cells by fat absorption, thus displacing the red marrow. Sometimes mixed marrow is mentioned. About the 15th year, the marrow in the large hollow bones is essentially yellow, remaining permanently red in some short, spongy and flat bones such as of the torso and the skull. According to Hedinger, red marrow is quite frequent in the femur of adults without any especial

disease being present, but Schridde thinks this requires microscopic verification, because red marrow might be only hyperemic yellow marrow, (see below).

Others differentiate soft marrow not held together by spongy bone trabeculae from spongy marrow, and according to color, soft red, soft yellow, spongy red and spongy yellow (comp. Helly and Kulbs). In very advanced age and in chronic diseases (early marasmus), jelly marrow appears, which is a gelatinous transformation of the fat marrow with a somewhat darker yellow color due to pigment cells (Ponfick).

In starved animals, Neumann always found gelatinous marrow as the fat disappeared and the cells resumed their original reticular form (see Jackson). The neutrophilic myelocytes are the predominant cells (Roger et Josue).

**The transformation of fat marrow into red marrow** (cell marrow) occurs in various pathological conditions, and the red marrow, where permanent, becomes hyperplastic (Schur and Lowy). Beginning from the epiphysis, red marrow may finally fill the whole cavity.

It is seen in oligemias, essential and secondary, (see under blood, p. 191 ff.). In pernicious anemia, the marrow appears like raspberry jelly and contains many early forms of erythrocytes especially megaloblasts, with diminution of granular cells in favor of myeloblasts, which are then in the majority (megaloblastic marrow).

The metamorphosis into red marrow has been proved in animals after phlebotomy and other experimental anemias. Young nucleated erythrocytes appear in larger numbers as a regenerative process (erythroblastic marrow is deep red). In the spleen, liver and lymph nodes, hemopoietic foci may also appear (lit. by von Domarus). In aplastic anemia (p. 193) on the other hand, the hematopoietic apparatus loses its power, and fat marrow is not transformed into red blood-forming marrow. As in experiments of Blumenthal and Morawitz who saw exhaustion of the bone marrow after repeated bleeding of animals, the organ showed no erythroblasts or granular leucocytes, but, wherever cell marrow was present, there were myeloblasts in abundance. Experimental destruction of bone marrow by x-rays causes a high grade leucopenia (see Heineke).

In various infectious diseases (see under IV) red metamorphosis appears, as Ponfick first showed in acute endocarditis. There is also marked production of myelocytes which appear in larger numbers in the blood (myelocytic marrow is grayish or red). [For details of the pathology of the bone marrow in anemias, see Peabody, F. W., Am. J. Path., 2–487, 1926, and 3–179, 1927.—*Translator.*]

**The Bone Marrow in Leukemia** (see p. 198 ff.).—As a rule in both forms of leukemia and even in pseudoleukemia (p. 205), the bone marrow

participates. It may be changed along with the spleen and lymph nodes, or alone with the spleen, or by itself, or predominantly so.

According to E. Neumann and Askanazy, there is no leukemia without changes in the marrow, but cases are known in which it was not involved, *e.g.*, in acute leukemia, (see Butterfield, Rehn), which shows that the development of myeloid leukemia does not necessitate a primary change in the bone marrow, *i.e.*, "myeloid" is not synonymous with "myelogenous."

In chronic lymphatic leukemia, the color of the marrow varies between dark red (raspberry jelly), pale red, and gray. The consistency is firmer, so that the observer can pull a marrow cylinder from the bone. Microscopically, the reticulum is recognizable, although very atypical, and contains many small lymphocytes, cell crowded against cell. This infiltration probably begins around vessels and is sometimes visible as macroscopic nodules which contain only lymphocytes; it then spreads, as a real entity, at the expense of myeloid tissue. Diffuse, or groups of lymphatic inclusions, as massed collections of lymphocytes are found in the bone marrow of acute lymphatic leukemia. The normal marrow disappears gradually, although larger or smaller remnants of myeloid tissue may remain (myelocytes, isolated giant cells, and erythroblasts), surrounded by masses of lymphocytes. This corresponds to a red or gray, moist, glassy, soft marrow (lymph adenoid marrow, E. Neumann). Most authors speak of its lymphoid character, but a reticulum presupposed by the conception "lymphoid," may be completely absent, being imitated, however, by a fibrin network.

In myeloid leukemia, the marrow is usually red, but sometimes grayish white or greenish (pyoid marrow, E. Neumann); nodules (see above) are absent. Microscopically, among the polymorphous cells (cell marrow), the myeloblasts and myelocytes and frequently the bone marrow giant cells, are increased. There are also colorless cells showing fatty degeneration, nucleated red blood cells, cells containing erythrocytes and, in contradistinction to lymphatic leukemia, many Charcot-Neumann crystals. The walls of vessels are frequently infiltrated by myeloid cells, (source of transference of cell to the blood).

Myeloid bone marrow gives a positive guaiac reaction (Brandenburg, R. Meyer). Tissue containing lymphocytes reacts negatively, but that containing leucocytes is positive. Smears made of blood, marrow, liver, spleen, lymph nodes give a positive reaction in myeloid leukemia. Like pus cells, they contain a ferment (oxydase) which oxidizes guaiacolic acid into guaiac blue; it is absent in lymphocytes, (oxidase reaction, p. 196).

Ponfick first pointed out hemorrhagic foci (infarcts) in the marrow of hollow bones, which he compared to similar changes in the spleen.

**Changes in Bone Marrow Due to Infectious Diseases.**—On account of its vascular supply, the bone marrow is very susceptible to invasion by bacteria, and experimentally, it has been shown that bacteria and insoluble dye substances injected into the blood (v. Recklinghausen) are partly retained in the marrow cells with remarkable increase of giant cells (comp. also under phagocytosis, p. 286). Pyogenic organisms produce so-called primary osteomyelitis; in miliary tuberculosis of the marrow which may be part of a general or a partial general miliary tuberculosis, organisms are retained in the marrow (more details under bones). In lymphogranulomatosis (see p. 267), nodules appear in the marrow (Eug. Fraenkel).

In different infections such as typhoid fever, pneumonia, small pox, etc., the marrow assumes a red color (Orth, Litten, Ponfick).

Eug. Fraenkel always demonstrated the specific organisms of typhoid fever in the red marrow of the vertebrae and ribs, and as special changes, foci of fibrin network, within which the bone marrow becomes necrotic (see under small pox). There is no numerical relationship between bacteria in the blood and in the bone marrow; the number demonstrable in the marrow is usually much larger. In pneumococcic and streptococcic diseases, especially erysipelas and scarlet fever, Fraenkel succeeded in demonstrating bacteria.

In the most varied local infectious diseases such as peritonitis, bronchitis, otitis media, ulcerative pulmonary tuberculosis, furunculosis, phlegmon, acute osteomyeletis, there may be invasion of the bone marrow, especially by staphylococci and streptococci. In all cases mentioned, the influx of bacteria may begin early and, especially in typhoid fever, remain after conclusion of the local process (see Wolownick, J. Koch).

Ponfick has also demonstrated fatty degeneration of small arteries and capillaries in various infectious diseases such as abdominal and exanthematous typhoid fever, intermittent fever, etc. In recurrent fever, the adventitia contains so many fatty granule cells, especially within the marrow of the diaphyses, that the arteries appear as chalky white, branching lines. Foci of finely granular disintegrated marrow (medullary foci of softening) are also found.

In malaria, pigment (see p. 210) is deposited in the marrow cells, while the marrow changes to red (Browicz).

In all these infections it must be mentioned that numerous cells containing blood corpuscles and pigment (iron) can be found in the splenic pulp, as shown by Ponfick.

As Chiari observed, in variola, there are multiple cellular marrow foci, up to the size of a half a pea, which later undergo central necrosis (variola osteomyelitis). Chiari described a similar specific involvement of the

testicle (see there). See Lossen, as to the condition of the bone marrow in diseases of children.

**Tumors of the Bone Marrow.**—In reference to specific tumors of the bone marrow—myelomas,— see under bone. There are also reports of primary and secondary sarcomas and carcinomas of the bone marrow; it must be emphasized that metastases of tumors primary in certain organs seem to have a special affinity for the bone marrow; see metastases from stomach, thyroid, prostate, and breast, especially carcinoma (see under enemia, p. 191), and also sarcomas (illustr. under thyroid), and malignant renal tumors (hypernephromas), etc.

## CHAPTER III

## RESPIRATORY ORGANS

### THE NOSE

**Anatomy.**—The nasal mucosa is classified as olfactory, respiratory, and vestibular; the latter lines the movable lowest part of the nose and is composed of pavement epithelium in layers, sebaceous glands, hair follicles (which are not rarely the seat of small furuncles) and vibrissae, (nasal hairs without errectores pili). The olfactory occupies the upper part of the nose within which the ramifications of the olfactory nerve—the olfactory organ—*i.e.* its terminals, are situated. The greater part of the respiratory mucosa, like in the accessory cavities of the nose, consists of layers of cylindrical ciliated epithelium as in the larynx and trachea, with some mucous-secreting goblet cells. This epithelium rests on a basement membrane. An extensive replacement of the cylindrical by pavement epithelium is frequently seen from meta- or hetero-plasia (Schoenemann). The lower mucosa contains lymphoid tissue often in large quantities. In the upper parts of the mucosa there is a capillary network; in other parts are found well developed venous plexuses which at the lower turbinates, with the addition of smooth muscle bundles, practically form erectile bodies. Many acinar glands are located in the submucosa with their ducts passing through the mucosa to the surface. The lymph vessels uniting at the posterior nares into larger trunks carry lymph to the deep cervical nodes and by way of the perineural lymph sheaths of the olfactory nerve, communicate with the subarachnoid lymph spaces (Key and Retzius, Flatau). This relation is important, since pathogenic organisms may spread through these channels (see also Zwillinger in reference to lymphatics).

**Malformations.**—Some are associated with cerebral malformations (see there); others are due to clefts in the facial skeleton; absence of, or proboscis-like malformations of the nose (with cyclopia) are rare. Occasionally, uni- or bilateral closure of the posterior nares and absence of the septum or of a turbinate are seen. Stenosis, unilateral, due to malposition of the nasal septum is more frequent. It is often accompanied by chronic coryza.

**Circulatory Disturbances.**—On account of the abundant supply of vessels, especially of veins, circulatory disturbances are extremely fre-

quent; congestive hyperemia may arise from any kind of irritation, and venous hyperemia from cardiac and pulmonary lesions, etc.

Epistaxis is due to many different causes; it may be traumatic after a blow on the nose, or congestive from hyperemia; or due to nasal catarrh, or vascular tumors (polyps), venous congestion (cardiac lesions), severe infectious diseases (esp. typhoid), and is habitual in constitutional conditions such as anemia, chlorosis, etc. In the hemorrhagic diatheses *e.g.*, hemophilia, scurvy and leukemia, the loss of blood may be dangerous. The blood is chiefly venous, and usually comes from the anterior part of the nasal cavity. In rare cases of typhoid fever, usually in the fourth week, ulcers appear in the lower turbinates, from which fatal hemorrhages have occurred from erosion of vessels.

In death from asphyxia in the newborn, hemorrhages of the nasal mucosa are of medico-legal importance.

**Inflammations.**—Simple Acute Catarrh, Coryza, Rhinitis, "Cold." The designation "catarrh" is derived from this frequent disease. The process begins with hyperemic swelling of the nasal mucosa, often with involvement of adjacent mucous membranes, such as the conjunctiva (first stage); exudation, partly serous, partly mucous, begins in the second stage; desquamated epithelium and leucocytes appear more and more abundantly, while the fluid, limpid at first, becomes thicker and mucinous.

The secretion contains ammonium chloride which causes swelling of the nares and upper lip and sometimes erosions, covered with scabs. Etiologically, various factors must be considered, such as mechanical, especially dust, thermic (see Schade: colds, he differentiates true from the much more frequent infectious colds or catarrhs); chemical, especially vapors of ammonia, nitric acid, iodine, osmic acid, etc., and infections, the latter of which may involve the nasal mucosa in infectious diseases either primarily or secondarily. Thus in influenza, measles, scarlet fever, erysipelas, small pox, exanthematous typhoid, etc., there is usually a nasal catarrh. Hay fever or catarrhus aestivus, appears in predisposed individuals and is probably due to the irritation of fine particles, or pollen grains of flowering grasses and other plants which reach the hypersensitive nasal mucosa, conjunctivae and bronchi with air currents. Others blame the disease on bacteria from hay, etc. The theory of pollen irritation seems correct (Dunbar, negative, Heymann and Matzuschita). The active factor is an albuminous, easily soluble substance, contained in the starch deposits (lit. by Wolff-Eisner). [For general review, especially in relation to anaphylaxis, see Coca, A. F., Arch of Path. & Lab. Med., 1, 96, 1926.—*Translator.*]

In the normal nasal cavity a number of known pathogenic bacteria are found such as the streptococcus pyogenes, staphylococcus pyoge-

nes, pneumococcus, pneumobacillus, etc., (lit. by Haslauer), which, although usually harmless, may become pathologically important if the mucosa is disturbed in its circulatory and secretory conditions by any irritant. The well known condition of "catching a cold" is explained etiologically as a factor in coryza. Kruse thinks that at least in one form of rhinitis and cough, the causative organisms are aphonozoae, *i.e.*, ultramicroscopic and filtrable viruses. See under lungs for the correlation between pulmonary inflammatory processes and nasal bacteria.

**Purulent Catarrh (Nasal Blemorrhea).**—This consists mostly of a surface secretion of pus; and only rarely of an infiltration of the mucosa, although the secretion is copious and offensive to the smell. Deep infiltration and suppuration of the mucosa is called a phlegmon. Etiology: Purulent catarrh may be caused by various primary or secondary infections, primary from common pathogenic organisms (staphylo-, and streptococci) and also from the gonococcus, foreign bodies, or from glanders. It may be secondary to measles, scarlet fever, small pox, true diphtheria of the throat, glanders, or operative procedures such as cauterization (comp. above statements, and nasal bacteria).

The communication of the lymphatics with the cerebral surface, as mentioned on p. 292, makes purulent nasal catarrh a dangerous condition; in some inexplicable meningitides a hidden purulent rhinitis may have been the starting point. The author saw purulent meningitis follow suppuration of polyps, and operations on nasal polyps. In such cases, a possible meningo- or encephalocele may also be present (see under brain).

**Pseudomembranous (fibrinous and diphtheritic) inflammations** are secondary to true pharyngeal diphtheria, scarlet fever, erysipelas and other infections, but may be primary.

The primary form of true nasal diphtheria (Loeffler-bacilli) is fairly common in the newborn and sucklings. Its course is usually mild, and it is often localized to one side of the nose (Ochsenius, Lande, Esch).

In true pharyngeal diphtheria, the whole nasal mucosa may be covered by pseudomembranes like a thick skin which sometimes may be pulled off as a complete cast, exposing a hemorrhagic mucosa. The mucosa may disintegrate into a discolored green necrotic mass.

**Chronic Rhinitis.**—Hypertrophic rhinitis. The mucosa and submucosa are thickened, first because of cellular infiltration, later by the formation of connective tissue. There is at times a large amount of purulent secretion, but the condition often remains in isolated parts of the mucosa (lower or middle turbinate) and polypoid thickenings appear. By metaplasia the surface epithelium changes into pavement epithelium.

Simple atrophic and fetid rhinitis is characterized by marked atrophy of the mucosa, and metamorphosis into fibrous tissue, poor in cells, in

which most of the glands have disappeared (Eug. Fraenkel). The atrophic form develops as a primary condition, or follows hypertrophic rhinitis when the soft cellular tissue is transformed to contracting connective tissue. Atrophy of the bony walls causes widening of the nasal cavities.

Fetid atrophic rhinitis, ozena vera, or simplex, is further characterized by a sweetish putrid smelling secretion, which dries into grayish green scabs on the pale, thin mucosa. The ciliated epithelium disappears, although not everywhere, and is replaced by layers of pavement cells, perhaps showing keratosis.

The peculiar penetrating odor is due to the inability of the few normally functioning glands to protect the secretion, itself odorless, from putrid decomposition (E. Fraenkel, Schonemann). It is well to remember, however, that putrid secretions may also result from suppuration of the antrum of Highmore, or syphilitic and tuberculous ulcerations, or necrotic tumors. The etiology of true ozena is much debated, (B. Fraenkel, A. Alexander); according to Meissner and Siebenmann, it is due to coincident metaplasia of the nasal mucosa in a broad nose, one of the symptoms of chamaeprosopy, (low face), which causes a slowing of the air current, stagnation of secretion, and drying into putrid crusts. But probably sufficient emphasis must be given to the inflammatory process causing atrophy, especially glandular atrophy. Others think the chief factor is a chronic empyema with necrosis of ethmoid cells (Rundstroem) and other accessory cavities (Amersbach); still others believe it is congenital lues (Fresc), or the lymphatic diathesis (Caldera), or preceeding inflammations, constitutional dyscrasias, physiological senile changes (Wright), etc. The so-called ozena bacilli can be found in healthy noses, and are supposed to be identical with the pneumobacillus of Friedlander (Fricke); they are probably not the cause of ozena, and are not found deep in the tissues. The theory of Perez that the cocco-bacilli of fetid ozena (Hofer and others) are the cause, also seems unable to stand critical investigation (comp. Caldera, I. L. Burckhardt and Oppikofer, lit.; see also discussion of ozena, B. 1918, 12, Berlin).

**Inflammations of the Accessory Cavities of the Nose.**—Simple and suppurative catarrhs may spread from the nose to adjacent cavities, frequently in acute catarrh, but also in chronic inflammations. They may progress to the frontal, ethmoid, and sphenoid sinuses (headache) and to the antrum of Highmore (bilateral, through the orifices in the middle turbinates).

Inflammation may also extend from the nose to the pharynx and through the Eustachian tubes to the middle ear (deafness, tinnitus); among other complications, suppurative otitis media may cause meningitis.

Milder or more severe inflammations of the accessory sinuses are frequent in the various infectious diseases, quite especially influenza (Eug. Fraenkel).

In the maxillary sinuses (of Highmore) the inflammation readily becomes chronic after the cause, nasal inflammation, has passed; it may be independent of the nose in origin, *e.g.*, in inflammations of dental roots (see teeth).

The unfavorable high position of the outlet in the nose, at the apex of a three cornered pyramidal cavity, makes it difficult for secretions to be evacuated and thus favors chronicity. By obstruction or narrowing of the orifice by polyps or swelling of the mucosa, retention occurs of the inflammatory products and thus there develops hydrops from the collection of sero-mucous secretion, which may be very abundant. Empyema is not uncommon; in both of these conditions the inelastic bony walls undergo pressure atrophy and bulge or even perforate, rarely in simple empyema, but more frequently in dental cysts and tumors. The perforation is through the anterior wall (canine fossa) into the nose, or into a dental alveolus (second premolar), channels selected by the surgeon to drain secretions. Even the frontal sinus, which occasionally extends far beyond the orbits (see Witt, lit.), may perforate, usually toward the nose, but also anteriorly (frontal skin phlegmon), or posteriorly (comp. Gerber, lit. and Onodi). In chronic productive catarrh, polypoid growths develop in the antrum, or metaplastic epithelium, and desquamated pavement epithelium, disintegrated into poultaceous masses, collect in large quantities. Sometimes single or multiple cystic polyps completely fill the antrum; according to P. Heymann (lit.), small tumors of this kind are quite common.

Trauma to the skull, even blunt force, occasionally allows pyogenic organisms to reach the meninges and meningitis results from hydrops and empyema of the accessory sinuses. Possibly small fissures open the way to the bacteria (comp. below), but it also occurs spontaneously, mostly from a periostitis. Brain abscesses, thrombophlebitis of the cerebral sinus (especially after empyema of the ethmoidal sinus), etc. have all been described (examples under brain).

**Translator's Remarks.**—Operative trauma occasionally releases bacteria to the meninges as in a 38 year old man who died of meningitis 4 days after operative procedures on the frontal sinus, the seat of chronic suppurative catarrh.

Orbital phlegmons have followed suppuration of the accessory sinuses. In a young girl, the author discovered that a nasal polyp was the cause of an empyema of the frontal and sphenoid sinuses followed by orbital

phlegmon, thrombophlebitis of the basal cerebral sinus as far as the jugular vein and meningitis. This complication also occurs in scarlet fever (Preysing).

See Kleijn, in reference to diseases of the optic nerve, usually axial neuritis, in inflammations of the posterior accessory sinuses of the nose.

When one of the air chambers is opened in basal fractures of the skull, latent organisms may reach the meninges and become active. Suppurative meningitis may also develop from indirect basal fractures in bullet wounds of the head, *e.g.*, in fissures of the lamina cribrosa of the sphenoid (v. Hansemann, Kanzow).

**Infectious Granulation Tumors. Granulomas.**—Tuberculosis is met with as (1) scrofulous rhinitis in which the mucosa is infiltrated with cells and covered by dried-up secretions (scrofulous ozena) over superficial ulcers. Occasionally, the deeper parts are affected, and perichondritis, periostitis and perforations of the septum and turbinates follow. Perhaps the secretion contains tubercle bacilli, at least, at times.

(2) True tubercle formation is rare, but occasionally appears as disseminated nodules in general miliary tuberculosis. Larger foci which ulcerate are secondary to diseases of the respiratory channels. Fungoid or polypoid tumors of tuberculous granulation tissue with giant cells and bacilli occur primarily, according to clinical statements. The author has received a number of such preparations for examination. Rapidly progressive granulations attack cartilaginous and osseous parts.

(3) Lupus extends from the skin to the mucosa, or, more often, in the opposite direction. Infiltrations of the mucosa, by preference in the anterior part of the septum and in the lower turbinate, are under granular warty excrescenses covered by thickened epithelium; these may coalesce, disintegrate, and finally heal into deep scars. Fresh nodules in the scars are especially characteristic. Lupus usually selects youthful individuals and females.

A peculiar affection occasionally observed, but not only in tuberculous individuals, is the perforating ulcer of the cartilaginous septum (Voltelini).

The ulceration begins in the anterior nasal septum, according to Hajek, from trauma (picking with finger), and hemorrhage into the mucosa. The tissue lesions release bacteria (common pyogenic organisms were found) which complete the necrosis and ulceration. According to others, it is tuberculous; it is known that tubercle bacilli may be directly inoculated by the finger (Koerner).

The typical septum perforation following "chrome ulcers" may be mentioned. It is very frequent in chrome workers, who do not sufficiently protect themselves by respiratory masks. It is a painless local erosion said to be due to inspired particles of chrome (Lit. Bamberger, Lehmann).

Syphilis is manifested in various forms: (1) primary syphilis of the nose is rare, exceedingly rare inside of the nose (vestibular). (2) Congenital syphilis may cause simple or suppurative chronic rhinitis, or atrophic rhinitis with ozena, but may also lead (3) to syphilitic infiltration of the mucosa in the form of flat or bulging papules which sometimes grow luxuriantly, obstruct the nasal space and disintegrate into ulcers.

The ulcers may extend, although rarely, outward and downward, invade the periosteum and perichondrium, cause extensive destruction, expose the bone and cartilage and lead to necrosis and expulsion.

(4) In late stages, gummas in the mucosa, periosteum or perichondrium ulcerate, and cause extensive destruction of the mucosa and the nasal skeleton.

Perforation of the cartilaginous septum causes no symptoms. When the entire septum is destroyed, both nostrils show as one hole and the tip of the nose hangs downward. When the cribriform perpendicular plate or the nasal bones are invaded, a saddle shaped sinking of the nasal bridge results. In advanced cases, the cartilaginous parts of the nose, including its tip, are pulled back over the bony parts, or the whole nose sinks into the pyriform aperture. In the most advanced cases, the greatest portion of the naso-superior maxillary skeleton is destroyed, allowing almost a fist to fill the cavity, often lined by suppurating soft tissues. An abnormal communication between the nasal and mouth cavities, through a perforation of the palate, is responsible for nasal speech. Necrotic fragments of bone and cartilage are expelled usually with little discomfort. During healing, the cicatricial contraction causes excessive external deformities and may lead to adhesions within the nose usually between the septum and turbinate and thus to stenoses and obliterations.

Glanders (malleus) is transmitted by the secretions of glanders-infected animals (horses, asses, mules). The portals of entry are lesions of the skin and mucous surfaces, or by way of the food, so it is dangerous to feed straw and hay soiled with bacilli-laden urine, or to use drinking pails contaminated by nasal discharges (Bonome), etc. Infection may thus result in the animals through the nose, but is more generally secondary, *i.e.*, hematogenous. The forms are diffuse infiltration (rare), or nodules consisting of closely packed epithelioid cells and leucocytes, the latter soon dominating the centers of nodules which undergo necrotic purulent disintegration, and liquefaction; the pustules then rupture and leave crateriform ulcers. Adjacent ulcers coalesce, new nodules develop in their peripheries, and also disintegrate; thus the ulcers assume very irregular forms. This is accompanied by a suppurative, often hemorrhagic, catarrh. The ulcers with yellowish bacony bases, are bowl-shaped and closely resemble tuberculous ulcers macroscopically. In chronic glanders, epithelioid cells are

quite abundant and for this reason, the specific glanders nodule is considered a link between a tubercle and an abscess (v. Baumgarten). They also invade cartilage and bone and when healing takes place it is seldom complete, for the process continues elsewhere and the raised cicatrices are similar to those of lues. The non-motile bacillus of glanders (Loeffler and Schutz, 1882), resembles the tubercle bacillus, but is somewhat larger and thicker. It is Gram negative (stained according to Kuhne). They are not always numerous, especially not in chronic glanders and their presence must be proved by inoculation into suitable animals. According to Straus, the best method is intraperitoneally above the bladder of male guinea pigs. The disease begins in 2 days with progressive swelling of the testes, due first to suppuration in the tunica vaginalis, then to nodules in the serosa, and in the testis itself. Death results in about 2 weeks, and nodules are found in various organs such as the lungs, liver and kidneys. Field mice are also suitable for this test (lit. by Wladimiroff-v. Baumgarten).

In the horse, acute glanders runs a course of from one to three weeks. The nodules and ulcers strung closely together appear in the skin and give it the name "worm" (French: farcin). The animals die from fever and weakness, and involvement of the maxillary glands, larynx, liver, spleen, kidneys, etc. Chronic glanders may last for years, but ends, as a rule, in death from cachexia, or from sudden exacerbations (comp. among others, Delbet and Chevassu, lit.).

The course of a fatal glanders infection (glanders pyemia) in man may be acute—two to four weeks; metastatic abscesses appear in the internal organs such as the lungs, spleen, bones and joints, especially the muscles, or pustular exanthemata develop in the skin (comp. Hubalek and Goldschmied, lit.). When chronic, it resembles that of horses; the nasal involvement and skin ulcers often regress with scar tissue formation but deep seated, boil-like tumors and joint involvements continue. Recovery is very rare. The clinical diagnosis is quite difficult (Luick, Stein). In one case autopsied by the author, death occurred in six weeks from transmitted purulent meningitis. She was the servant of a veterinary surgeon and had cleaned the trousers of the doctor after they had been soiled from an autopsy on a horse which died of glanders. Among other findings, foci were detected in the lungs.

Leprosy also causes nodular granulomas with a tendency to ulceration in the nasal mucosa. According to Sticker, the nose is the chief portal of entry for the infection, and the leprous ulcer which discharges large numbers of bacilli is the first symptom, and the chief source of infection (comp. Schaeffer). Gluck could not verify this in detail, and Gerber and Babes do not support this view. On the other hand, Field found ulcers

in the nose in 85% of tuberculous and leprous mixed cases, and considers the nasal secretion the source of infection. According to Kitasato, apparently healthy wives of leprous men frequently have lepra bacilli in the nasal mucus and thus possibly act as carriers. In the course of the disease, perforation of the septum, sinking of the bridge and collapse of the nose are not rare.

Rhinoscleroma is caused by a bacillus described by v. Frisch in 1882. It is an indurating infiltration which begins in the nostril or in the mucosa at first without swelling; it extends to the nasal alae, oral aperture and further; in the course of years it develops painless tumors, sometimes lobulated with cicatricial contractions about the nostrils and mouth, sufficient sometimes to almost completely occlude the former. Rhinoscleroma is relatively frequent in Austria, but it also appears in Italy, Russia, Switzerland, (lit. by von Schulthess, Nager); in Germany it is more frequent in eastern Prussia and Silesia.

Microscopically, even with low power, the so-called Mikulicz cells can be seen between closely packed small round cells. These are clear large cells with honeycombed structure; any stain will serve. According to v. Marschalko, they are the characteristic, specific elements of the scleroma; according to earlier statements they are connective tissue cells, according to Schridde, plasma cells, which constitute the main mass of the tissue and which undergo mucoid degeneration due to invasion of the bacilli, or to distant toxic action. They also develop vacuoles and larger spaces, show nuclear pyknosis and swell considerably. These foamy, hollow cells comparable to the so-called lepra cells, contain bacilli, often in enormous numbers; when overfilled, they rupture, and the bacilli pour out freely into the tissues where they slowly perish. These irregularly formed, large, colorless cells remain visible for a long time, but are later replaced, as a rule, by an hypertrophic collagenous tissue which gives to the scleroma its characteristic hardness. Konstantinowitsch (lit.) considers certain hyalin bodies characteristic. These are the so-called Russel bodies (or fuchsinophiles, since they retain the fuchsin in Russel's double stain of fuchsin and iodine green); they are also frequently present intraepithelially or extracellularly in carcinoma and have been interpreted by Sanfelice and others as coccidia, but are viewed by most authors as products of cell degeneration and necrobiosis. They are seen in sarcomas also (comp. v. Muller, lit.), are constantly found in the company of plasma cells and within them, frequently in inflammatory processes (lit. by Miller and Alagna). They stain red with eosin and straw yellow with van Gieson's stain. In rhinoscleroma they are supposed to be formed in endothelial cells from absorbed erythrocytes; Schridde, following the precedent of Unna and v. Marschalko, believes they are derived from plasma cells, a

statement which the author supports. Schridde, furthermore, thinks they are derived from neutrophilic granules which change into acidophiles.

Scleroma bacilli are morphologically and culturally closely related to the bacillus of Friedlander (see under lung); indeed Paltauf considers them weakened Friedlander bacilli. The encapsulated organisms stain well with Gram stain (the Friedlander b. is decolorized very quickly), and are not, or but slightly virulent for experimental animals (mice, rabbits, guinea pigs). Besides this, according to Gerber, their specificity is still uncertain (comp. Kraus).

Scleroma is found primarily in the naso-pharyngeal or laryngo-tracheal mucosa, from which it invades neighboring parts. Respiratory scleroma is another designation. The tissue seldom suppurates (Rona), but has a tendency to cicatricial changes. Therapeutic measures to date are useless. In the larynx, the lower part is selected, and usually symmetrically, for the growth of grayish white or pale red, finely granular or smooth, firm, even cartilaginous infiltrations, which, in severe cases, change the larynx into a hard, stenosed canal (Jieffinger). Membranous scars may also form. It may then extend to the trachea and bronchi. Rona demonstrated the presence of viable bacilli in regional lymph node masses (Lit. in reference to rhinoscleroma by Babes; also Goldzieher and Neuber, Gerber, Nagy, Nager, Sternberg).

**Tumors of the Nose and Its Accessory Sinuses.**—Benign Tumors. Without regard to histological structure, circumscribed, usually soft, pedunculated, often multiple tumors, frequently on the turbinates, are called nasal polyps.

To the first group belong polypoid overgrowths and hyperplasias of the mucosa, soft, essentially of similar structure as the mucosa, but more markedly cellular; their color is red or grayish red.

Alagna calls them granulomatous polyps; they often consist almost exclusively of plasma cells (plasmocytomas, page 272).

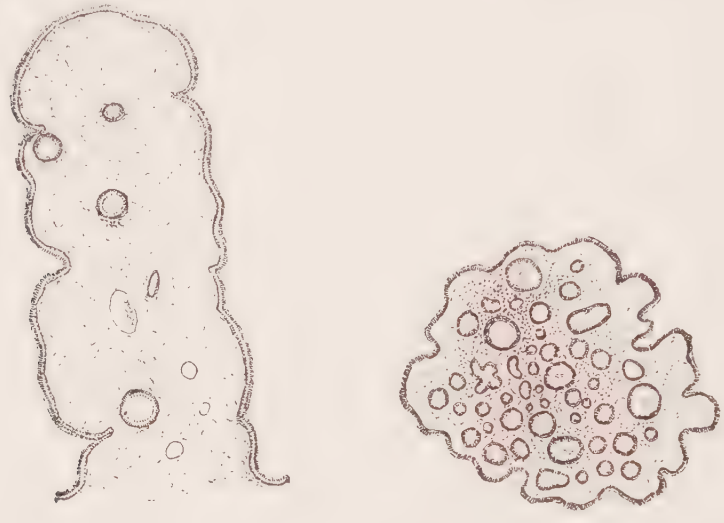
Adenomatous polyps or flatter hyperplasias of the mucosa, adenomatous vegetations, with active new development of glands, are grayish red and opaque (fig. 142).

Cystic polyps result from retention of secretions in mucous glands enclosed in the overgrowths; they are glassy and transparent.

Some polyps look like raspberries with villi; they are papillary polyps, or papillomas.

Differentiation is made between soft polyps covered with epithelium and situated chiefly on the lower turbinates, and hard, really tumor-like papillomas, usually attached to the nasal septum, and covered with several layers of pavement epithelium (papillary fibroepitheliomas). The former are benign, the latter are clinically malignant and may become papillary

carcinomas. Herxheimer (lit.) described a rare, hard papilloma of the frontal sinus covered with cylindrical epithelium (cylindrocellular papillary fibroepithelioma).




FIGS. 141–142.—A, Myxomatous nasal polyp, girl 7 years old; 1cm. long, pale yellow, translucent, mucoid, soft. Cross section, margin consists of several layers of ciliated cylindrical cells; predominant substance mucous tissue; within this, some cross cut vessels and gland ducts. B, Adenomatous nasal polyp from a young woman; 0.2 cm. high, gray red, opaque, soft; cross section shows margin of cylindrical cells; stroma shows marked small cell infiltration and contains numerous glands (both low power).

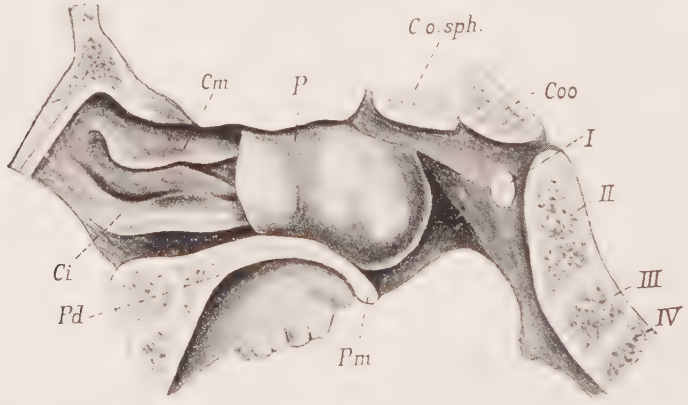



FIG. 143.—Large nasal polyp (edematous vascular fibroma) inserted on sup. turbinate of 8 year old boy. Death from purulent meningitis. P, polyp; Ci, inferior turbinate; Cm, middle turbinate, above which the anterior part of the sup. turbinate is visible; Pd, hard palate; Pm, soft palate; Co sph, sphenoid bone; Coo, occipital bone; I, II, III, IV, corresponding cervical vertebrae; ⅘ nat. size.

A second group is of pedunculated polyps, mucoid, jelly-like, yellowish, transparent structures, often multiple, pear, drop, or globule shaped and varying in size (fig. 143). Some are polypoid myxomas, some are polypoid

edematous fibromas. They occur chiefly on the middle and superior turbinates.

On account of their mucoid consistency, they are simply called mucous polyps, but this name is not always correct in a histological sense.

Polypoid myxomas consist of true myxoma tissue, *i.e.*, meshes, formed by cell prolongations, filled with mucin-containing fluid which coagulates on the addition of acetic acid (fig. 141).

Edematous fibromas consist of a meshwork of alveolar connective tissue (Hopmann) containing serum, albumen and round cells. Heymann also found elastic fibers. Glands disappear in these connective tissue tumors. Alagna calls them serous polyps. If the meshes are big, it is a so-called vesicular or cystic polyp. Some are vascular (angiomatous polyps), others show many dilated vessels (telangiectatic); firm fibromas are rare (covered by cylindrical or pavement epithelium). Other benign tumors are: chondromas (Schwerdtfeger, lit.), osteomas, osteofibromas, dermoids, lymphangiomas (Szmurlo, lit.), all of them rare. Chondromas prefer the upper part of the nasal cavity. The tumors mentioned may also start in the accessory sinuses, especially in the antrum of Highmore and thus cause malformations of the nose and the facial skeleton, especially broadening.

Nasopharyngeal polyp is the name given to fibromas, which frequently do not arise in the nasal cavity, but from the base of the skull, the anterior part of the vertebrae, or the walls of the naso-pharyngeal space and its immediate vicinity, such as in the sphenopalatine fossa (Koschier), usually from periosteum or from fibrocartilage. They are differentiated into intra- and extrapharyngeal. The latter first attract attention as retro-maxillary tumors. Nasopharyngeal polyps grow toward the frontal or ethmoid sinuses, or downward into the nasopharyngeal cavity; they crush whatever bony tissues oppose their growth, force themselves into adjacent cavities, and sometimes produce severe facial malformations. Retro-maxillary tumors endanger the orbital cavity by invasion. They rarely have a true pedicle and secondarily grow into the soft tissues and bone. They are often very cellular and vascular (vascular fibromas, fibroangiomas). They are also mixed with sarcoma (fibrosarcomas) and the differentiation of cellular fibromas from sarcomas is not always easy. Usually they occur in younger males from 10 to 25 years of age, although the author saw a fibrosarcoma in a 7 year old girl, which grew to the size of a hen's egg in four months.

**Malignant Tumors.**—Sarcomas of the nose are usually spindle cell, round cell, or angio-sarcomas (lit. Sonnenschein); occasionally, melano-sarcomas are found (Cozzolino, lit. Schumann). The author saw one of the latter in a 73 year old woman, who had suffered for a long time from

nasal obstruction, and for the last five weeks from severe epistaxis. It presented itself in the left lower nasal tract, and consisted of rounded and angular, partly pigmented, partly necrotic cell masses. The so-called endotheliomas have also been described but most of them are probably epithelial cylindromas (Alhoff, lit., Tilley, Trautmann, Spangenberg, Pollak, lit., Pfeiffer). Sarcomas may start anywhere in the nose; the inferior turbinate is favored, or the accessory sinuses (Krogius, lit.). The author has seen cylindromas of the ethmoid, *i.e.*, of the antrum, structurally similar to that of fig. 104, in a 64 year old woman, and a 40 year old man, and a large round cell sarcoma in the antrum of a 51 year old man. Round cell sarcomas grow quickly with a tendency to spread out flat, and often attack younger individuals. Sarcomas of the epipharynx have secondarily infiltrated the nose, as the author saw in a large round cell sarcoma in a soldier. Plasmocytomas which select the nasopharyngeal mucosa must not be mistaken for sarcomas.

Carcinomas are usually of the soft cylindrical cell type (Cordes, lit.), and may take the form of a highly organized adenocarcinoma, as the author saw in two cases. Usually they spring from the vestibular region. Keratosing, or non-keratosing squamous cell carcinomas, also, frequently start from the mucosa of the respiratory region when the cylindrical epithelium previously changes to squamous cells (pp. 292 and 294), or when metaplasia occurs in the tumor itself; in the first case, pavement epithelium can usually be seen beyond the carcinoma (lit. by Trautmann). Cylindromatous basal cell carcinomas (see above) are quite frequent, while papillary carcinomas are rare. Isolated secondary nodules are sometimes seen. Carcinoma may also start from the accessory sinuses (rare). A carcinoma of the skin or the pharynx may secondarily invade the nose.

**Translator's Remarks.**—The prognosis of carcinomas depends, at least to a certain extent, on the type. The translator has seen two highly organized adenocarcinomas in men 38 and 45 years of age, operated 7 and 9 times. Each time a recurrence appeared, it was removed. Both patients eventually died (5 years), the one of meningitis, the other of cachexia with clinical metastases in the lungs. On the other hand, a man of nineteen died ten months after the onset of symptoms. The latter tumor was a cornifying squamous cell carcinoma which proved utterly refractive to all forms of therapy. For carcinoma of the maxillary antrum, see Hansen E. W., Journ. Lancet. 45: 105: 1925.

**Rhinoliths and Parasites.**—Rhinoliths are lime deposits around foreign bodies (beans, cherry stones, cotton plugs), or in and around thickened secretions, and may have angular, pronged, or shell-like shapes.

They are often the cause of suppurative and putrid catarrh; when situated in front of a tubal orifice they cause difficulty in hearing. Botey described one 110 gms. in weight.

Parasites. Occasionally animal parasites are seen. Myiasis—deposits of fly eggs—is seen principally in the tropics. Plant parasites are harmless saphrophytes or pathogenic bacteria (p. 293). (Lit. Pathology of the nose by Suchannek, E. V., 1901 and VIII, 1904 and X, 1906. Onodi, Path. and Ther. d. Nasenkr. Wien, 1910 with good anatomical pictures.)

## LARYNX

**Anatomy of the Larynx, Trachea and Large Bronchi.**—The cartilaginous scaffolding of the larynx is chiefly hyalin. Elastic cartilage forms the vocal process of the arytenoid, Santorini and Wrisberg cartilages, and the epiglottis. (Elastic cartilage is present elsewhere only in the ear.)

The mucosa is of stratified ciliated cylindrical epithelium, resting on a basement membrane with the exception of the true vocal cords, the edges of the false vocal cords and the lower surface of the epiglottis; these are of stratified pavement epithelium. The mucosa contains lymphoid cells, in some places (posterior surface of the epiglottis, sinus of Morgagni and their appendages) also diffuse adenoid tissue and follicles, and rather numerous plasma cells (comp. Imhofer). (The ramifying appendages with their enclosed lymphatic tissue are also called the laryngeal tonsil, B. Fraenkel, Imhofer, lit.) In the upper layers of the mucosa of the lower (respiratory) part (conus elasticus) of the larynx are elastic fibers (v. Cyzlarz, Przewoski), in the lower part, mucous glands. In the true vocal cords, the mucosa consists of elastic fibers, arranged in the direction of the cord; there are no mucous glands. A loose submucosa with numerous mucous glands is found at the lower surface of the epiglottis, the aryepiglottic ligament, the false vocal cords, and over the arytenoid cartilages.

Blood vessels (branches of the sup. and inf. thyroid artery) and lymph vessels ramify in the subepithelial layer of the mucosa.

The epiglottis and the true vocal cords have microscopic papillae.

The arched cartilaginous rings of the trachea are closed posteriorly by bundles of smooth muscle fibers. The cross section of the trachea in the living is almost cylindrical; in the cadaver, it is flattened posteriorly. The length of the trachea in the male to its bifurcation is 12 cm., in the female 11 cm.; by extension, *i.e.* stretching of the neck, it may be increased one third its length. In the outermost fibrous layer of the bronchial walls there are cartilaginous plates more or less regularly distributed, but the cartilage gradually decreases in the small and microscopic ramifications of the bronchial tree. The ciliated cylindrical epithelium of the larger

bronchi consists, like that of the trachea, of several layers; in the smaller tubes but one layer is present. It is superimposed on a structureless membrana propria; the other structural design is essentially similar, but a connected layer of circular smooth musculature is added in the bronchi between the mucosa and the fibrous layers. (Details of musculature of the lungs and pleura by Baltisberger.) Mucous glands are less numerous than in the trachea, are located in the outer fibrous layer and are gradually lost with the cartilage plates where the finer branchings of the bronchial tree enter the lobules of the lungs. The diameter is then less than 1 mm. The loose mucosa contains many blood vessels and a rich lymph vessel network which communicates in the submucosa with that surrounding the pulmonary blood vessels. (For anatomy of the bronchial tree, see Aeby, Narath, topography by Stoerck.)

### Malformations of the Larynx

Individual cartilages may be absent or insufficiently developed. The larynx may be abnormally small, sometimes associated with a high pitched voice; it remains small in the castrated in whom the voice is high, and the pitch breaks as in a growing boy (see Habock). Congenital atresia of the larynx due to early fusion of both laryngeal embryonic buds is quite unusual, (lit. by Frankenberger and Krosz). It is also rare to find congenital membrane formation due to embryonal epithelial adhesions, in the form of a diaphragm, usually at the anterior commissure of the vocal cords or below, with more or less broad ends behind and a crescent shaped free rim (lit. by v. Bruns, Glas). Sometimes symptoms are entirely absent (hoarseness, falsetto voice, aphony, dyspnea). Heredity has been suspected. Congenital membranes or folds on the posterior wall of the larynx are still rarer (Fein, Frankenberger). Nakayama described a double membrane on the posterior wall; it has been observed twice on the anterior wall. Ulcerative processes, especially syphilitic, may result in acquired membranous adhesions. Occasionally, the appendages of the false vocal cords are abnormally large and extend to the extralaryngeal air sacs (ventricular laryngocele, Virchow). On pressure and coughing, such laryngoceles are visible from the outside as air-containing sacs. If the tumor bulges inward, it may cause much difficulty. (For other important observations in reference to laryngocele, see R. v. Hippel and Reich, lit.) An exceptional congenital laryngeal cyst is considered by Schneider (lit.) due to the snaring off of a ventricle, *i.e.*, appendage; it caused death by suffocation in a female 26 years of age (see case of Punder).

### Circulatory Disturbances

Active hyperemia is not important in a pathological anatomical sense, but clinically, it is frequent and deserving of notice. It is caused by over-

exertion of the voice, gases, dust, heat. After death the hyperemic redness disappears almost completely because the elastic fibres of the mucosa retract and exert pressure on the vessels. In pregnant women, a change occurs in the larynx which has been called vaso dilator swelling, increasing at times to real edema (Imhofer). Inflammatory changes considered essential by Hofbauer, are incidental findings according to Imhofer, and are not essential histological findings. Imhofer could find no decidual changes.

Passive hyperemia results from general congestion, such as from cardiac and pulmonary lesions, or local factors such as tumors compressing the laryngeal veins. The mucosa appears bluish red. Pronounced filling of the veins may lead to phlebectasia and this to hemorrhage.

FIG. 144.—So-called edema of glottis; laryngeal opening markedly narrowed by inflammatory edematous swelling of the ary-epiglottic lig. of 42 year old man with ulcerative tuberculosis of lungs and larynx; inferior tracheotomy; $^{9}/_{10}$ nat. size.

Hemorrhages in the otherwise unchanged mucosa occur in suffocation, in scurvy, hemophilia, Werlhoff's morleus maculosus, poisoning (phosphorus), and various infectious diseases (hemorrhagic small pox, typhoid fever, etc.).

**Edema of the Larynx.** (Glottis.)—This is serous infiltration of the submucous connective tissue, resulting in a yellow jelly-like dense swelling. It appears chiefly at the upper part or laryngeal entrance where the submucosa is loose, *i.e.*, the upper surface of the epiglottis, the false vocal cords, the area above the arytenoid cartilage, and especially the aryepiglotteal plicae. Swelling of the latter causes them to meet in the midline and obstruct the laryngeal entrance; if swelling of the false vocal cords is added, the trachea is also occluded (fig. 144). The edema is often only partial.

The designation "edema of the glottis" is incorrect, since the glottis (rima glottitis) is not the site of the edema. It is better to say "epiglottis edema."

The fluid partially or completely evaporates after death; the regions lose their dense appearance and become wrinkled, folded and slack.

Acute edema of the larynx, if extensive, is clinically of great importance on account of the imminent danger of suffocation. The symptoms are increasing inspiratory, later also expiratory, dyspnea, and laryngeal stridor. Asphyxia can be prevented by incising the swollen mucosa, or by tracheotomy or intubation.

In a 30 year old man with a phlegmon of the anterior portions of the neck, the author saw laryngeal edema involving the lower part of the epiglottis which had formed a ring as broad as a finger with the edematous piriform pharyngeal sinus; stenosis from swelling caused suffocation.

Acute inflammatory edema often develops quite rapidly and occurs:

1. In conjunction with local affections such as traumata, pointed foreign bodies, fish bones, scalding, (as the author saw in a small child, from drinking hot tea), cauterization from poisons (*e.g.*, lysol), or from ulcerating diphtheritic processes of the larynx.

2. From extension of inflammatory processes in the vicinity, such as pharyngitis, diphtheria, tonsillitis, peritonsilar phlegmon, parotitis, erysipelas, suppuration of lymph nodes with surrounding phlegmons, vertebral caries.

3. It may be secondary to severe infections such as scarlet fever, small pox, sepsis, pyemia, cholera, typhoid fever, anthrax.

Acute edema develops occasionally in iodism (idiosyncrasy), from the internal use of potassium iodide (iodine-edema, comp. Fournier).

Chronic inflammatory edema develops in chronic inflammatory processes of the larynx, is usually partial, and rarely reaches a high degree. The case, fig. 144, is rather rare, but in ulcerating tumors it causes attacks of suffocation.

Non-inflammatory chronic edema (serous saturation) is usually due to congestion as a part of general hydrops, in chronic renal or cardiac diseases, cirrhosis of the liver, or pressure exerted on the veins of the neck by tumors of the neck, goiters, aneurysms, etc. It rarely reaches as high a degree as in acute inflammatory edema, but sometimes in general dropsy with increasing cardiac insufficiency it is the final fatal catastrophe.

### Inflammations of the Larynx

**Catarrhal Inflammation, Laryngeal Catarrh.**—(1) Although acute catarrh is very frequent, it is seldom evident in the cadaver. When present, it is recognized by redness, swelling, and sparse muco-serous or muco-purulent secretion. The mucosa is involved in spots or diffusely. Occasionally, there are superficial epithelial lesions, the so-called catarrhal erosions, which continue the incentive to coughing.

Etiology.—Acute catarrh of the laryngeal mucosa develops primarily from various irritations such as chemical (gases), thermic (hot or cold air), mechanical (dust bacteria); secondarily it occurs in infectious diseases such as measles, scarlet fever, small pox, typhoid fever, syphilis, etc.

Pertussis bacilli, small organisms discovered by Bordet and Gengou, appear in vast numbers, and practically without admixture of other organisms in the expectorations and in the laryngeal mucosa as a part of the laryngo-tracheobronchial catarrh and bronchopneumonia of whooping cough (lit. re bacillus of pertussis in appendix), (see under brain for pachymeningitis, leptomeningitis and encephalitis hemorrhagica with pertussis).

In influenza (see p. 341), laryngeal catarrh is one of the symptoms of a specific inflammation of the entire respiratory tract. (See p. 312 for laryngeal inflammation in diphtheria.)

**Chronic Catarrh.**—The secretion in chronic catarrh becomes tough and scanty, and occasionally dries into crusts. The mucosa is red from

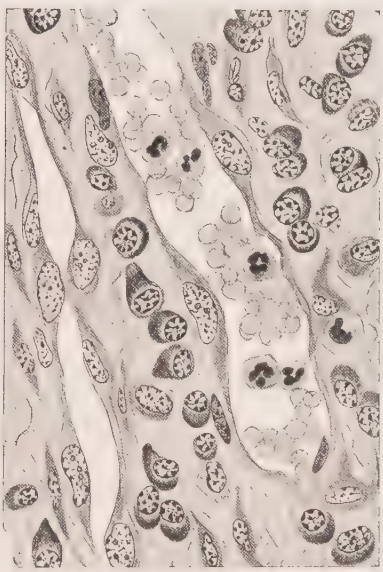


Fig. 145.—Plasma cell infiltration of mucosa in laryngeal pachydermia; two blood capillaries (in one red blood corpuscles and leucocytes) with thick endothelium; in the surrounding connective tissue (fibrillae and fibroblasts, spindle-shaped or with several prolongations) numerous typical plasma cells (wheel-spoke form of nuclei and eccentric position with a light halo surrounding it); see p. 9.

filling and distension of its blood vessels, becomes hypertrophic, rough, and uneven, but sometimes becomes atrophic. The thickening depends on cellular infiltrations with many plasma cells (fig. 145), and connective tissue elements which sometimes produce papillary proliferations (Stoerk).

When the enlarged, distended mucous glands bulge as glassy nodules, the condition is called "granular" laryngitis, sometimes mistaken for miliary tuberculosis.

The epithelium is infiltrated by round cells, the ciliated cylindrical epithelium changes into pavement epithelium, or proliferates with thickening and cornification (epidermoid change). The latter is seen on the true vocal cords. Thickened epithelial layers are sharply differentiated from the reddened adjacent tissue, as bluish or milky white coatings readily pulled off (diffuse pachydermic laryngitis, Virchow). Sometimes the thickened epithelium produces a papillary mucosa proliferation as

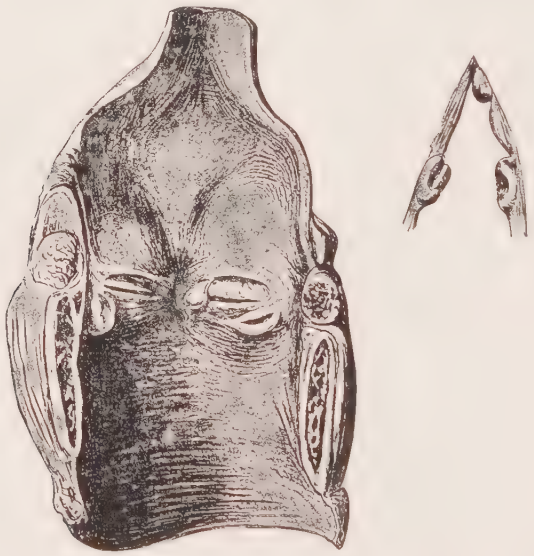


FIG. 146.—Diffuse laryngeal pachydermia; to left, humps on true vocal cord with depression; right, a corresponding depression with raised margins; fibrous polyp in r. ventricle of Morgagni. The small illustration shows the vocal cords from above; in the corner the polyp. Man 63 years old. Death due to fracture of skull; 5/6 nat. size.

the "inflammatory papilloma" of the clinician, situated chiefly on the anterior part of the vocal cords (pachydermia verrucosa, Virchow, as in fig. 154; see p. 321).

Etiologically must be considered: occupational diseases which demand greater exertion of the organ and chronic assaults by impure atmospheres. Drinkers and excessive smokers very often show pharyngeal and laryngeal catarrh.

Diffuse pachydermia on the posterior sides of the vocal cords at the vocal process may produce symmetrical ovoid bulgings on one side and cup-shaped depressions on the other which fit together, or two symmetrical

oval indentations develop lipped margins which fit into each other (fig. 146). The hollows are caused by mutual pressure, (abrasion, Rethi), are white and often show minute fissures (rhagades). Carcinoma may develop in pachydermia (comp. B. Frankel).

Another form of chronic inflammatory proliferation resembles plasmocytomas (see p. 272 and 301).

**Pseudomembranous Inflammation of the Larynx.**—Superficial croupous and deep diphtheria. (Many still use the poorly constructed term "diphtheritis" instead of diphtheria.)

1. Croup is a simple inflammation with a pseudomembrane consisting essentially of fibrinous exudate, covering the red, small cell-infiltrated mucosa as a pale white layer which becomes thicker from layers added from below.

The membrane may cover the laryngeal surface completely or in disconnected patches and sometimes as a tubular cast firmly attached to the vocal cords and continuing through the respiratory part of the larynx into the trachea itself (fig. 147). The false vocal cords are often bridged or partly filled and the membranes may occlude the vocal aperture. They have the consistency of tough fibrin and are 1 to 2 mm. thick.

Microscopically, the membrane consists of several layers of delicate fibrin fibrillae, and a close network of shiny, thick fibrinous columns, enclosing hyalin necrotic epithelium which can be recognized only at the beginning of the membrane formation. The number of pus cells varies in the several layers and in individual cases (fig. 162).

FIG. 147.—Pseudomembranous laryngo-tracheitis by continuity from true pharyngeal diphtheria; margins of epiglottis free; interior of larynx thickly lined; in the trachea the coating is partially lifted off as a tube; man 39 years old; $\frac{2}{3}$ nat. size.

The epithelium dies and disappears in the fibrinous mass which takes its place. The mucosa beneath shows an acute catarrh; lymph and blood vessels also contain fibrin; the mucous glands show various changes such as hypersecretion and dilatation, inflammatory edema, leucocytes and fibrinous exudation, swelling, necrosis, epithelial exfoliation, etc. (see Borel).

Usually, the membrane may be easily pulled off, especially when over ciliated epithelium; it may also be detached spontaneously by a layer of pus, but it may reappear.

2. The more penetrating form of pseudomembranous inflammation in diphtheria is better called "diphtheritic inflammation" in the anatomic sense; it is less common in the larynx than the simple form. Part of the mucosa becomes necrotic and participates in the formation of the membrane by combining its tissue with the fibrinous exudate. It looks like a solid glassy cast of cloudy pale gray to grayish yellow color. If the membrane is detached, the so-called diphtheritic ulcer is uncovered.

Differentiation between croupous and diphtheritic (necrotizing) inflammation. In both the epithelium is lost, is necrotic and disintegrates during the formation of the pseudomembrane. On the margins, the solidifying exudate may overflow intact epithelium. In croupous inflammation the membrane is superficial (solidifying exudate), and can be pulled off from the mucosa without loss of substance, *i.e.*, it is a simple fibrinous or a superficial pseudomembranous inflammation. In diphtheritic (necrotizing) inflammation the necrosis and fibrinous exudation are combined, and part of the mucosa is incorporated with the membrane. Croupous and diphtheric inflammation differ only in degree, and both may be present at the same time.

The membrane is always more firmly attached to the parts lined with pavement epithelium even if no actual diphtheritic inflammation is present, for the reason that the epithelium does not rest on a basement membrane like ciliated epithelium, and the fibrin which absorbs the epithelium comes in intimate contact with the mucosa.

**Etiology.**—Pseudomembranous laryngitis develops in conjunction with true primary pharyngeal diphtheria. (See under pharynx in reference to the cause of diphtheria—Bretonneau's diphtheria,—the Loeffler diphtheria bacilli.) The larynx is rarely the primary site of the disease, and then only over the areas covered with pavement epithelium; when present, the process usually continues into the trachea, even to the bronchi and lungs, where it is followed frequently by lobular atelectasias and bronchopenumonia.

In other cases, croupous or diphtheritic inflammation is secondary to another infectious disease (lit. Oppikofer), and is then not due to Loeffler's bacillus, but usually to strepto- or staphylococci. The membranes are thinner and do not consist of as many layers as in true diphtheria.

In influenza, pseudomembranous, fibrinous, and perhaps encrusting laryngo-tracheo-bronchitis is seen; the larynx is grayish yellow, as though tanned (Marchand), or covered as with bran (see Watjen). Common pyogenic organisms are found.

After thermic or chemical irritation such as scalding with hot steam, burning gases, local cauterization, gases such as ammonia, war gases (see W. Koch), swallowing of corrosive substances, in uremia, etc., a primary pseudomembranous, frequently purely croupous, laryngitis is found. Otherwise a primary laryngeal croup is very rare (Schech).

Result.—When superficial croupous laryngitis heals, perfect regeneration is accomplished, and the epithelium is renewed from the remaining cells. Diphtheritic inflammations heal by granulation tissue and scars, but when the larynx participates in pharyngeal diphtheria, the necrobiotic process is so superficial that cicatrization is slight and no traces are left. When the necrosis extends to deeper layers, however, (in recurrent cases), stenosing scars may result.

C. Phlegmonous inflammation. Abscesses.

A coagulable sero-purulent or true purulent exudate of yellowish to yellowish green, hazy color is deposited on the mucosa and in the submucosa. The regions mentioned in laryngeal edema are also favored in this inflammation which may actually follow the inflammatory edema. If the tissue itself suppurates within some circumscribed area, an abscess is formed.

In a case of pyemia following umbilical thrombophlebitis, Imhofer (lit.) described multiple metastatic abscesses in the laryngeal muscles without involvement of the submucosa.

Phlegmonous inflammation follows trauma, ulcerations, inflammations, diseases of the vicinity, especially erysipelas of face or neck, severe tonsillitis, etc., or is hematogenous in infectious diseases. Not rarely a perichondritis is developed with pus collections between the cartilage and the perichondrium; the latter is lifted and the cartilage perishes in part or in toto. If the process is rapid, the cartilage is unchanged externally as a sequestrum in the pus cavity; otherwise it becomes shredded and rough or undergoes purulent liquefaction. Perichondritis is thus analogous to periostitis.

**Etiology.**—Perichondritis usually joins an existing ulcerative process (tuberculosis, syphilis, typhoid fever), or is hematogenous in origin without previous ulceration, as in pyemia, small pox, typhoid fever, etc.

The arytenoid cartilage is the most frequent one involved because its mucosa is the favorite locality for tuberculous ulcers. In the arytenoid perichondritis of typhoid fever or tuberculosis (fig. 149 P. a.), the cartilage sequestrum lies in a cavity from which fistulae penetrate into the larynx. The cartilage may be expelled through such a fistula either whole or in fragments; it is then expectorated, or reaches the lower air channels or remains in the larynx. If the fistula is narrow and the cartilage is separated, it remains in the cavity. Only occasionally will a fistula perforate externally (perilaryngeal abscess), or into the esophagus.

The cricoid cartilage, especially its plate, among other causes, is involved in pharyngeal decubital necrosis (fig. 279), the arytenoid cartilage, especially from syphilitic ulcers, or marginal ulcers, in which difficulty in deglutition may occur. Marginal ulcers are due to decubitus of the mucosa which covers the cartilage, and are relatively frequent in typhoid fever (fig. 148) or, as seen by the author, in the general edema of lead poisoning, contracted kidneys, retroperitoneal puerperal abscess, diffuse bronchitis. Moreover, in a young man who was cachectic from long continued forced antisyphilitic treatment, the author saw an extensive ulcer which occupied the free edge of the epiglottis from which the denuded cartilage bulged upward. There were also extensive decubital ulcers on the skin of the elbows, the shins, the pelvic spines, the sternum, Adam's apple, etc. Specific, *i.e.*, tuberculous, ulcers appear but rarely as marginal ulcers. In thyroid perichondritis, larger intralaryngeal pus pockets may develop, rupture and cause suffocation.

FIG. 148.—Marginal ulcers of epiglottis in typhoid fever; $^5/_6$ nat. size.

Perichondritis due to syphilis and suppurating carcinomas may cause sequestration of almost all the cartilages, so that the larynx becomes a flabby sac, and collapse may cause sudden death. Comp. p. 327.

### Pathological (Usually Ulcerative) Processes in Specific Infections

**Tuberculosis.**—Tuberculosis of the larynx is extremely frequent, often combined with chronic ulcerative pulmonary tuberculosis, and consequently chiefly seen in adults.

It is probably due in most cases to infection by sputum, perhaps after a chemical lesion of the mucosa has been produced by erosive action of the sputum (see experiments of Albrecht and Dold). Some believe a secondary infection is possible by way of the blood and lymph channels. Tuberculosis of the larynx may be primary (inhalation), but it is certainly much more frequent clinically than anatomically (Manasse, Steiner, lit.).

According to the external appearance, several forms are recognized, but, of course, the classification is not perfect and does not cover all cases.

(*a*) Lenticular ulcers, beginning on the surface, are often superficial for long times. They originate as small miliary tubercles under the mucosa and undergo caseous necrosis, thus forming a surface lesion, the erosion or ulcer. They usually disintegrate before they can be observed macroscopically. At first, the ulcers are shallow indentations, easily overlooked at

autopsy; they may be made more distinct by washing blood over them. They are lenticular in shape, with fairly distinct but flat edges, and usually have pale yellow gray bases. At their margins and below, new nodules appear and disintegrate; thus the ulcer increases in size and depth (fig. 149), becoming confluent and forming figures bordered by the segments of circles so that they may eventually involve the entire larynx. Thus the lenticular character is lost. As the ulcers become deeper, their bases show caseous masses and nodules, their edges are pronged and raised, finally, they may penetrate the cartilage (perichondritis). The chief point of election of these

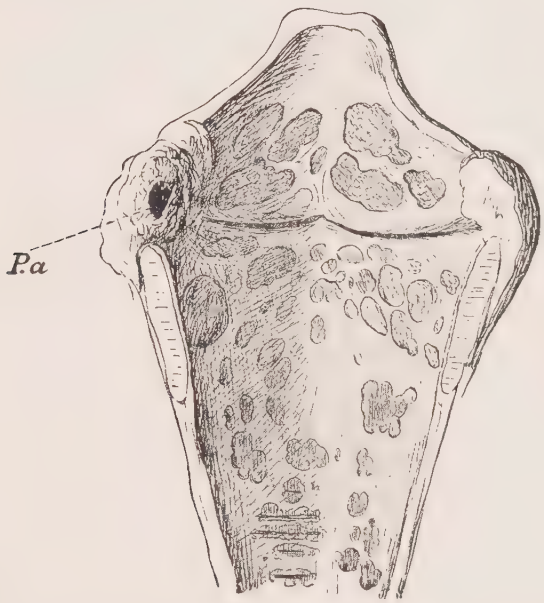



FIG. 149.—Numerous tuberculous lenticular ulcers in larynx and trachea; arytenoid perichondritis (P.A.); empty cavity; the cartilage is thrown off. In the trachea some cartilaginous rings are exposed and necrosed by ulcers. From a phthisical girl.

lenticular ulcers is the inner surface of the epiglottis. The so-called aphthous ulcers in ulcerative pulmonary tuberculosis are inflammatory lesions combined with necrosis started by streptococci; they must be mentioned for diagnostic reasons. Tubercle bacilli may of course secondarily find a foothold in them (comp. Ziba, lit.).

(*b*) Tuberculous infiltrates occur in the depths of the mucosa and disintegration quickly causes deep ulceration. A firm bacony mass is seen in which the yellow spots (caseous foci) contain tubercle bacilli. Sometimes the tuberculous infiltration starts in the follicles and if disintegration takes place, there appear deep irregular ulcers with eroded edges and uneven bases covered with caseous purulent material.

They locate where there is a loose submucosa and considerable follicular tissue (epiglottis, false vocal cords, above the arytenoid cartilages). Perichondritis follows, and fistulae are common.

According to Eug. Fraenkel, secondary invaders such as staphylo- and streptococci help in the further development of the ulcers.

(*c*) Ulcers running a chronic course which show a tendency to become perichondrial, are often located on the arytenoid cartilage (vocal processes). They are very deep and have hard margins. The true vocal cords also frequently show chronic ulcers, oblong and slit-like, sometimes deep enough to almost divide the cords, *i.e.*, with apparent duplication, or perhaps extensive enough to completely destroy them (aphonia). The vicinity of the ulcers may show a milky white thickening of the pavement epithelium.

The formation of nodular, polypoid excrescenses of the mucosa is rarer and is produced by massive subepithelial development of tuberculous granulation tissue. The course is usually chronic. Ziegle calls this form "hypertrophic" laryngeal tuberculosis, but it is more correct to say "hyperplastic." Occasionally tumor forms are mentioned, when well circumscribed formations give the clinical impression of mucous polyps or fibromas, etc.

The interarytenoid region is selected, but as in other forms, such overgrowths occasionally occur in other parts, *e.g.*, in the upper parts (the author). If caseation and disintegration take place, irregular ulcers result and sometimes actual polypo-fibrous mucous overgrowths are present besides the ulcers. Portmann calls these tumor-like forms, rich in connective tissue, "fibro-tuberculomas."

Lupus, a variety of tuberculosis, involves the larynx secondarily to lupus of the face or pharynx. Females before puberty are preferred. Soft, polypoid excrescenses and thick nodular plates are easily mistaken for carcinoma. Ulceration occurs, or scar tissue is deposited, within which small, brownish red excrescenses are likely to redevelop. The scars may cause deformities. These ulcers, differing from the common tuberculous ulcers, have neither markedly infiltrated surroundings, nor a caseous base. The course is chronic and the epiglottis is favored (mistaken for lues). It is questionable if lupus develops primarily in the larynx (lit. by Chiari and Riehl., Garre), but Siebermann was the first to describe a lupus pernio (see under skin) of the upper air channels.

**Syphilis.**—Syphilis of the larynx occurs in the secondary and tertiary stages. There are: (*a*) milder involvements in the early stage of syphilis in the form of catarrh without specific manifestations, or of somewhat raised white papules of the mucosa (papular laryngitis) which leave erosions and shallow ulcers on disintegration.

Microscopically, the papules show cellular infiltration of the mucosa and often an epithelial thickening. They may recede, or after loss of the epithelium, become erosions or somewhat deeper defects or ulcers with gray coatings; they usually remain superficial and heal without much scar tissue. Deeper ulceration and perichondritis are rarely found.

(*b*) The more severe involvements in the later stages of syphilis are composed of gummas, some as diffuse hard infiltrates in the superficial layers, which may ulcerate and disintegrate, and some as firm nodules beginning chiefly in the submucosa, in rare cases of sufficient size to close the lumen. If they undergo caseous softening and fragmentation, there result variable, often more or less circular, kettle-shaped, deep ulcers with bacony bases and sharply demarkated infiltrated rims.

When numerous, the whole mucosa is undermined and even perforated, having only small strips of mucosa bridging the ulcerations. At times, the epiglottis is perforated. Extensive caseous or suppurative perichondritis and necrosis of cartilage frequently occur. (Danger of edema of larynx.) Erosion of the laryngeal artery and fatal hemorrhage are rare, but have occurred.

These lesions frequently involve also the tongue and pharynx, but appear selectively in the upper part of the larynx, especially in the epiglottis, which may be as large as a small nut if it contains a larger gummatous nodule. As a rule, it is ulcerated at autopsy as though nibbled or bitten and cicatrized. Other parts are drawn into the involvement, notably the vocal cords.

If the ulcers heal, it is with the formation of firm, retracting scars, elevated, ridged, and often arranged in delicate knitted patterns. Between the scars, callused, thready or irregular bulging tissue bridges remain (fig. 150) (bridge scars). Sometimes fibrous bridges are also caused by adhesions between opposite ulcerating surfaces. See illust. of scars of the trachea, p. 333.

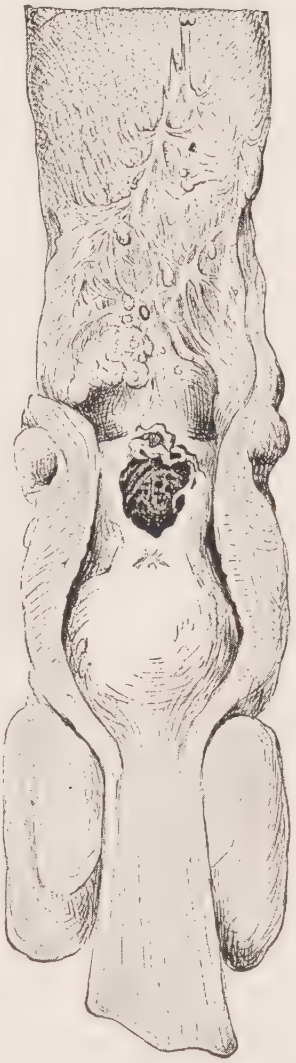


FIG. 150.—Healed syphilitic ulcers of larynx and tongue. Syphilitic stenosis of the laryngeal opening. Epiglottis completely gone with exception of some fibrous lumps. Numerous scars in larynx. Cicatricial changes of the base of the tongue with partial smoothing, alongside large superimposed radiating scars. Female, middle life; 9/10 nat. size.

The occasional finding of scars, lesions, and fresh ulcerations all at one time is quite characteristic of syphilis.

Ulceration and formation of scar tissue cause the most extensive deformities, especially stenoses of the laryngeal aperture (figs. 150 and 151), or within the organ, and the lumen may be completely obliterated. This can occur of course only if a previous tracheotomy has opened an air passage. On the other hand, small gummata may heal by absorption without leaving scars.

Besides these diffuse and large nodular infiltrates and the cicatricial processes, condyloma-like, papillary proliferations are found occasionally

FIG. 151.—Retroflexion of a perforated epiglottis in lues. Cicatricial ridge within the larynx, smooth atrophy of base of tongue in which only a few granular papillae are left. Woman of 51 with syphilitic aortitis; death due to rupture of an aneurysm, as large as a pea, of the basilar artery; $\frac{5}{6}$ nat. size.

on the remaining areas of mucosa, especially on the epiglottis. The latter may be bent forward (anteflexion) due to scar tissue retraction, quite frequently according to Hansemann, and substantiated by the author. But it occurs also without syphilis from regressive changes in the cartilage of the epiglottis (Lindemann). Adhesions of the latter to the base of the tongue occur from lues as well as from traumata (G. Fischer). The author observed a case of acute angular retroreflexion of the epiglottis in a woman 51 years old with very advanced smooth atrophy of the tongue (fig. 151).

**Typhoid Fever.**—This infection causes a variety of lesions, due to the typhoid bacilli or other organisms such as pyogenic cocci, chiefly staphylococcus pyogenes, or a combination of both.

(*a*) Catarrhal inflammation in typhoid fever leads quickly to erosions which may end in deeper ulcers. Ecchymoses also occur.

The ulcers are located chiefly along the sharp rim of the epiglottis; their edges are rolled inward and the cartilage of the epiglottis is exposed in their bases (fig. 148, p. 314). They are decubital, for the edematous swollen mucosa, almost directly covering the cartilage, is especially adapted to this type of change. By progressive perichondritis, the epiglotteal cartilage can be peeled out almost completely. As a preparation in the collection at Basle shows (illustr. by C. E. E. Hoffmann), it was a long, discolored, rolled structure hanging to the retracted integuments. As a rule, pyogenic cocci can be cultivated from the lesion.

(*b*) Medullary swelling of the lymphoid tissue, especially of the follicles, is analogous to the intestinal changes in typhoid fever and like these, are, according to Eppinger, an effect of typhoid bacilli. Ulceration and perichondritis may be diffuse or circumscribed. The favorite location is the posterior wall of the epiglottis, and the false vocal cords. Hemoptysis and laryngeal pneumatocele, starting from ulcers, are described by Marchand as an unusual complication of typhoid fever.

(*c*) Mycotic necrotizing inflammation. Deposits like bran are found in the beginning, and according to Eppinger, are not exudative inflammatory products but the result of epithelial necrosis due to bacteria (mostly staphylococci). Later, shallow ulcers appear with firmly attached delicate coating in which the superficial layers of the mucosa have also been destroyed. Eventually, a deeper ulcerative destruction may reach the cartilages (perichondritis). The location of ulcers is in the rim of the epiglottis, posterior laryngeal wall and vocal processes.

In the most severe manifestations of influenza, an analogous laryngo-tracheo-bronchitis may appear due to staphylo- or streptococci.

(*d*) Diphtheritic, but non-specific inflammation (see p. 312).

(*e*) Primary perichondritis of the thyroid, cricoid, or arytenoid cartilages, *i.e.*, without previous ulceration, is rare (see p. 313).

**Small Pox.** In this infection, there are general inflammatory changes causing reddening of the mucosa or the formation of diphtheritic membranes, or bran-like coatings consisting of desquamated necrotic epithelium and leucocytes, thickly covering the laryngeal or tracheal mucosa. Small nodules or pseudo-papules reach the dimensions of hemp seeds (Eppinger); they formerly were considered true small pox pustules but they are merely necrotic epithelial masses, infected, and infiltrated by leucocytes. Disintegration of the nodules and pustules causes the formation of small round ulcers; pronounced destruction is, however, rare. In later stages small pus foci sometimes appear deep in the tissue. In the hemorrhagic form, (black small pox), hemorrhages are added.

**Leprosy.**—The larynx is often involved by way of the pharynx. Leprous granulomas (lepromas) disintegrate, become ulcers and may even-

tually heal, leaving dense stenosing scars. The changes are somewhat similar to those of syphilis and lupus. According to Bergengrun, the epiglottis is always involved.

**Glanders** is rare. The disease is generally transmitted from above; subepithelial nodules appear and become ulcers.

**Scleroma** of the larynx often selects the subglotteal region (see under nose p. 300).

**Actinomycosis** of the larynx may follow actinomycosis of the head and neck; it is unusual (Hoffmann, Natzler, lit., Lessing). It also appears as a primary condition (Behr).

### Tumors (Relatively Rare)

**Benign Tumors.**—Mucus polyps are small, soft or hard, more or less vascular tumors corresponding to the mucosa in their architecture (hyper-

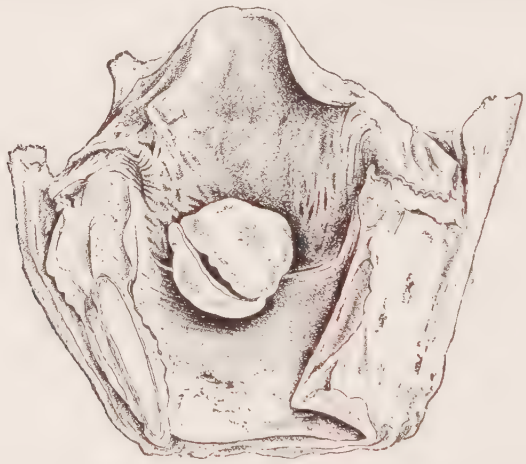


Fig. 152.—Cystic polyp size of a hazel nut, attached by broad base to left false vocal cord; on section cheesy detritus was emptied. Man of 65 died during an attack of asphyxia. So-called suffocation position of epiglottis, gutter-shaped curving; $^{9}/_{10}$ nat. size.

plastic polyps), or to glands which participate actively in the formation of the tumor. They are soft and lobulated, and occasionally become cystic from edematous saturation, myxomatous metaplasia, or from ectasy of glands (mucous polyps, cystic polyps). Glandular ectasia with increase in glands gives rise to simple cystic polyps as seen on the true vocal cords.

Cystic polyps are relatively rare. They locate especially on the false vocal cords and their ligaments. They may reach the size of beans or hazel nuts. Sudden death by suffocation has been caused by their prolapse from a sinus of Morgagni into the lumen of the larynx (fig. 152). (Lit. in ref. to laryngeal cysts by Ulrich.)

Papillomas or papillary fibro-epitheliomas. The papillomas of the clinician are the most frequent neoplasms of the larynx. They appear

chiefly at the lower surface or anterior commissure of the vocal cords in the form of granular, berry-like, small, red tumors, often with a broad base on the vocal cords, or as cauliflower-like, multiple proliferations which may cover the greater portion of the internal larynx. In children, these are almost the only tumor occurring in the larynx (fig. 153).

There is danger of suffocation, either from filling of the larynx by the tumor itself, or from cicatricial stenosis following operative removal.

Some papillomas result from chronic inflammation (comp. p. 309); probably the case illustrated in fig. 154 is one of these.

Fig. 153.

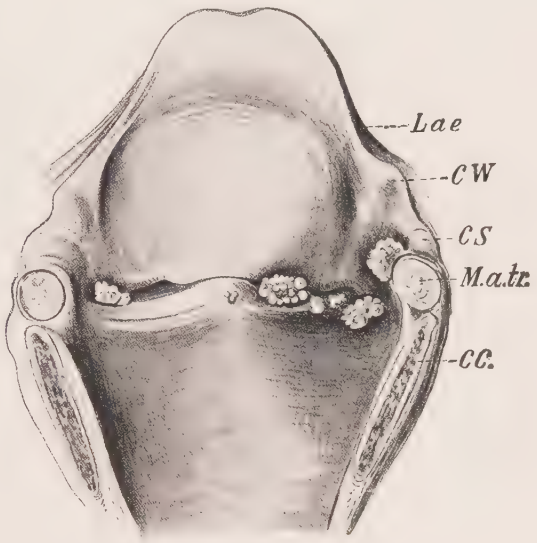



Fig. 154.

Fig. 153.—Numerous thickly grouped so-called papillomas (papillary fibro-epitheliomas) in the upper part of the larynx of a child, covering the vocal cords; suffocation position of epiglottis; nat. size.

Fig. 154.—Multiple so-called papillomas in various places of the laryngeal mucosa of 65 year old washerwoman. Lae, ary-epiglottic lig.;—Matr, transverse arytenoid muscle;—CC, cricoid cartilage plate;—CS, Cartilage of Santorini;—CW, Cartilage of Wrisberg; nat. size.

They often recur quickly after removal, either in loco or elsewhere in a previously healthy place due perhaps to inoculation. The patient with the tumor illustrated in fig. 156, came every few months to have his larynx cleared of numerous papillomas.

Histologically (fig. 156), they consist of a ramifying connective tissue core with vessels, often quite wide, and of a delicate or thick pavement cell covering sharply demarkated from its base and showing a cylindrical cell layer (basal cells) which stains more deeply; cornification is frequent. In well preserved specimens numerous mitotic figures in the epithelium can always be found. The papillomas are covered with pavement epithelium if they spread over wide areas, otherwise with cylindrical epithelium, but

they develop mostly in situations where there is pavement epithelium and papillae.

A varied nomenclature is encountered such as: papillary fibromas, condylomata acuminata (Ziegler), papillary epitheliomas (Orth); the

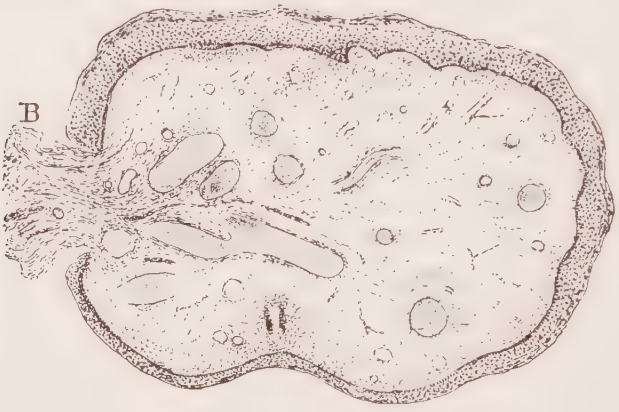



FIG. 155.—Soft vascular fibroma of left true vocal cord with unequally thick layer of pavement epithelium, partly cornified. B, base of tumor; (low power).

author calls them "papillary fibro-epitheliomas," expressing both the important part played by the thick layered epithelium in which proliferating processes by mitosis are recognized especially in the lower layer, and the part assumed by the connective tissue which is distinguished by its

FIG. 156.—Papillary fibro-epithelioma from the false vocal cord of a man, delicate papillary fibrous core; papillae covered with thick layer of pavement epithelium (no cornification); B, base of tumor; adjacent are three groups of acinous glands; (low power).

great number of blood vessels, but which, in contradistinction to verrucose pachydermia, is very poor in cells. For the histological differentiation from carcinoma, see p. 324. A squamous cell carcinoma can develop in a long existent papilloma, as in the case illustrated in fig. 158. It may also develop earlier.

Nodular fibromas (fig. 155) are soft or firm, semiglobular, pear-shaped or spherical, small and solitary polypoid tumors, with broad bases or pedicles. Next to papillomas, they are the most frequent laryngeal tumors. Most of them are located on the vocal cords and appear relatively frequently in singers and children (singers' nodules, childrens' nodules). Usually they grow quite slowly, and often remain stationary.

Very vascular fibromas approach angiomas in structure. Usually no glands are present. The participation of small cell infiltration, epithelial thickening, edematous saturation and hyalin degeneration is variable (comp. H. Cordes).

Angiomas, usually cavernous, (lit. by O. Hirsch, Roux), more rarely pseudoangiomas, or a varix in the form of a nodule, myxomas, solid adenomas of the mucous glands, lipomas, chondromas (lit. by Mansfeld, Roos), or ecchondroses—tumors springing from cartilaginous scaffolding, of the size of a hemp seed to a pea or larger—and mixed forms such as fibromyxochondromas, etc., are rare.

Mistakes in diagnosis may be due to: goitrous thyroid tissue within the larynx or trachea, (lit. appendix), or to the so-called amyloid tumors; both are unusual. The latter are differentiated into (a) infiltrating, (b) nodular, broad based, or polypoid pedunculated forms (Manasse, Glockner). The tissue is hard as wood, but glassy and transparent, and nodules have been seen as large as cherries (Schrank). In a case of the author in Basle (illustration by Johanni), the amyloid tumor was spread out like a plateau in the larynx and reached into the trachea; it caused laryngeal stenosis; the diagnosis was carcinoma. In a case of Reich, the tracheal amyloid tumor was radically removed by operation. In a second case at Basle (see S. Saltykow), the small globular tumor was accidently found at autopsy.

These are purely local amyloid conglomerations, principally in the lymph vessels, tissue clefts and vessel walls (comp. C. Hueter, Herxheimer, lit. and Hofmeier). In the case of v. Werdt, local amyloid was found in the whole respiratory tract; in other cases coincident so-called amyloid tumors of the buccal pharyngeal cavity were encountered (Willimann, Seckel, Pollak). Amyloid degeneration is rare in true tumors such as fibromas or sarcomas (comp. Burow, Manasse, Uffenorde and others). Plasmocytomas may resemble tumors and sometimes grow in the mucosa of the upper air channels, (Hoffmann, lit.; Kusunoki-Frank, and p. 272).

**Malignant Tumors.**—Sarcomas are rare. They may be of the spindle cell or polymorphocellular variety. They are rounded or nodular, of firm consistency, with nodular surfaces and relatively slow growth. Metastases into the lymph nodes are usually late. Round cell or alveolar sarcomas are soft and have a tendency to disintegrate (perichondritis);

they have broad bases, light to dark red color and quickly infiltrate the lymph nodes. Giant cell sarcomas are rare. Manasse described endotheliomas. Clinically, they are easily mistaken for tertiary lues (gummata and perichondritis). The vocal cords may remain intact. Males are more frequently affected. Lymphosarcomas are rare (fig. 157), but may be primary or secondary from the pharynx as diffuse, pale firm infiltrations which narrow the laryngeal aperture especially when in the epiglottis and the ary-epiglotteal ligaments. Infiltration of the lymph nodules of the neck is early. They are similar to leukemic infiltrations and aleukemic adenia, or simple adenia (fig. 277). Menzel described, as a unique case, a malignant hypernephroma of the larynx; Pfeiffer, a cylindroma (comp. p. 181) of the laryngeal entrance; Marchand a cylindroma (epithelial) in the interior of the larynx, and Ullmann a carcinosarcoma.

Fig. 157.—Narrow laryngeal opening caused by lymphosarcoma, to which is also due stenosis within; started from pharynx; woman 62; ⅔ nat. size.

Primary carcinomas spring mostly from the epithelium of the true vocal cords; when secondary, they are a continuation of a lingual, pharyngeal (fig. 278) or tracheal (rare) tumor. Occasionally a carcinoma starts from glandular epithelium (cylindrical cell).

Semon differentiates internal and external laryngeal carcinomas; the external variety is less common and has a bad prognosis. It arises in the epiglottis, ary-epiglotteal ligaments or the esophageal side of the larynx. The internal tumors are prognostically good when removed early; their favorite starting point is the true vocal cords, more rarely the false vocal cords, or the ventriculus of Morgagni or the depth of the larynx. Laryngeal carcinoma is much more common in males (Sendziak, Semon); but the author has seen a number of cases in young women.

The typical laryngeal carcinoma is of the cornifying squamous cell type. The microscopic picture is dominated by quite atypical epithelial proliferations, in the shape of plugs or columns anastomosing with each other. There are numerous mitotic figures and commonly, although not always, they show exceedingly abundant, concentrically arranged epithelial pearls. On the other hand, the interstitial tissue, often markedly infiltrated—the mucosa is rich in plasma cells—sometimes recedes.

If the so-called papillomas, removed by cauterization or burning, are examined, there can be observed an astonishing polymorphy and atypical structure of the epithelium almost to the point of carcinoma. The essential factor in differentiation between them and carcinoma is nonpenetration of the epithelium into the depths and perhaps also a minor

amount of proliferation of the cells of the rete mucosum. To differentiate from diffuse pachydermia the main factor to be considered is the dissolution of the cancer bodies into small plugs and groups of atypical cells, without basal cells, which enter deeply, as if isolated, into the connective tissue. Small cell infiltrations are found in both.

The development of carcinoma is often preceded by harmless small polypoid or papillomatous elevations, and at times by a pedunculated tumor (comp. Burger) or a flat infiltrate, usually on the true vocal cord, which soon becomes unequally nodular (hoarseness). Gradually the carcinoma infiltrates the depths at the location of the tumor and interferes with the motility of the vocal cord. The infiltration may extend to the false vocal cord and involve the other side also. Later, often only after

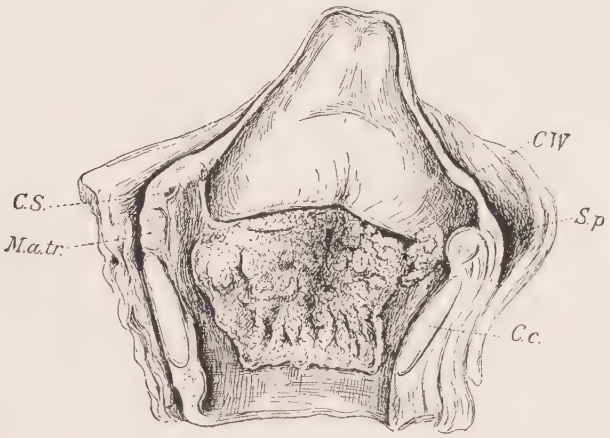



Fig. 158.—Carcinoma of larynx, granular, lumpy, man of 46 years; cornifying squamous cell carcinoma. At posterior part of r. vocal cord is a lumpy papillomatous excrescence (histologically also simple papilloma); began 23 years before as so-called papillomas (published by Barth, A.f.L. 7 Vol. and investigated anatomically by the author). CW, Cartilage of Wrisberg in the ary-epiglottic lig.; CS, Cartilage of Santorini;—Matr, transverse arytenoid muscle;—CC, cricoid cartilage;—SP, piriform sinus; 4/5 nat. size.

some time, the neoplasm breaks down, an ulcer appears, pyogenic organisms enter, and the tumor masses invade the vicinity destructively without respect for tissue boundaries (even to the pharynx and esophagus). Papillary excrescences may grow from the base of the ulcer. Necrotic disintegration, hemorrhages, stenosis from tumor masses, or more frequently and earlier, acute edema occur, as seen by the author in sudden death of a 57 year old man. The carcinoma resembled that in fig. 158. Perichondritis may cause sequestration of almost all the cartilaginous parts and thus the larynx becomes a flabby sac of integuments. The danger of suffocation and necrotic aspiration pneumonia is always present, as in a 27 year old woman, not operated. Nothing was left of the larynx

except a piece of epiglottis; one year previously a tracheotomy had been performed for edema of the larynx thought due to laryngeal tuberculosis. Metastasis occurred only in the submaxillary glands and death occurred from pulmonary necrosis. It is easily mistaken for tuberculosis; the author, *e.g.*, examined fragments of a papillary squamous cell carcinoma, coughed up by a 26 year old woman, and a small piece of tissue removed for diagnosis from a 20 year old girl which was also squamous cell carcinoma. In both cases the clinical diagnosis was tuberculosis.

The variations of squamous cell carcinoma are: the easily bleeding villous, so-called cauliflower type; the medullary, vascular and cellular, soft, quickly growing and quickly disintegrating nodular form; and the so-called scirrhous carcinoma, a squamous cell tumor relatively poor in cells, firm, with marked development of connective tissue, and less tendency to decay.

For development from papillomas, see p. 325 (fig. 158), and from pachydermia, see p. 310; otherwise the etiology is obscure (Semon). Local combinations with lupus or tuberculosis are rare, *e.g.*, the cases of Crone-Baumgarten, Franko.

Metastases.—Laryngeal carcinoma (internal) is often a local affection for long times, with a favorable operative prognosis. Metastases are rare except in the cervical lymph nodes and these appear only after a long time. When the submaxillary nodes are involved, however, the carcinomatous masses spread and proliferate with great rapidity. The author has seen two cases with metastases in the liver, and in a 61 year old man, the skin of the neck extending to the shoulder contained numerous, yellow, firm metastatic nodules the size of half a lentil.

Carcinoma of the external parts of the larynx soon gives rise to regional and general metastases.

### Trauma, Foreign Bodies, Parasites

Individuals from 30 to 40 years of age in whom the hyalin cartilage is calcified—a process which begins at the twentieth year—are more predisposed to fractures than younger persons. In osteomalacia, the author found the larynx of a woman 48 years old without a trace of ossification macroscopically or microscopically; in a 64 year old woman (see illust. under bones), only a few small bone nuclei were present; in a 68 year old woman ossification was confined to but few areas. (This latter case was briefly published by Siebenmann.) In cretins, the laryngeal skeleton may be cartilaginous in the sixth decade (Zieleniewska-Stefanoff).

Ossification begins where skeletal growth stops, in the thyroid cartilage at the posterior side of the plate, on the cricoid cartilage on the plate

(details by Chievitz, Scheier, Eug. Fraenkel, also pathological ossification by Dreifuss). In the aged, the hyalin cartilage is changed into spongy bone. Fibrous cartilage does not change. In fractures, the submucous hemorrhages, and simple or inflammatory edema may cause sudden asphyxia. The thyroid and cricoid cartilages are the most frequently fractured.

Foreign bodies cause decubital ulcers; even relatively small foreign bodies, especially sharp bone splinters, may prove fatal, from edema of the glottis and spasms of the rima glottidis. Sometimes they are lodged for a time within the larynx, especially in the pockets of Morgagni, but may reach the trachea and bronchi. Some exceptionally large, *e.g.*, false teeth, occasionally pass through the larynx and slip into the trachea. A large morsel of food (usually meat, bits of potato, etc.) during hasty eating or from a deficient masticating apparatus, may block the laryngeal entrance in front, over it, or become wedged within it. Suffocation may follow swiftly (comp. Oppikofer, lit.). For intubation trauma and its consequences, see p. 336. Laryngeal calculi occur in rare cases in the sinus of Morgagni from incrustation of secretion and epithelium.

**Parasites.**—In trichinosis, the organisms invade the laryngeal muscles quite early. Ascaris during the vomiting of gastric contents have been known to reach the larynx and in rare cases, cause suffocation.

## TRACHEA

(Normal anatomy, on page 305.)

### MALFORMATIONS

(Lit. by Schneider, malformations of the respiratory organs.)

Normally the bifurcation of the trachea is at the level of the sixth cervical vertebra. The first branch from the right main bronchus leads to the right upper lobe and lies above the pulmonary artery (right branch); it is called the eparterial branch. The branch which leads to the bronchi of the median and lower lobes lies below the artery. There is no eparterial bronchus on the left side.

A second eparterial branch may emerge from the main bronchus somewhat higher up; indeed this accessory branch may be placed so high as to spring to the right from the trachea itself. When it is rudimentary with a blind end, it is presented as a congenital tracheal diverticulum (Chiari); ciliated epithelial cysts in the mediastinum (see under thymus) and thyroid (Isenschmid), and accessory lungs (see p. 359 under lungs), are considered as originating in snared off parts of the respiratory

tract. For more details in reference to tracheoceles, larger air containing sacs, uni- or bilateral in the anterior part of the neck, see Petit.

Abnormal congenital communications between trachea and esophagus are called esophago-tracheal fistulae (internal fistulae). In reference to this and other malformations involving both the trachea and the esophagus, see under esophagus (figs. 280–282).

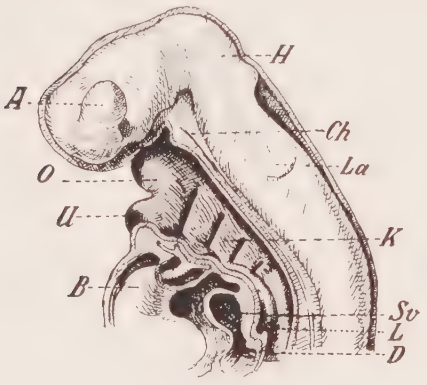



FIG. 159.

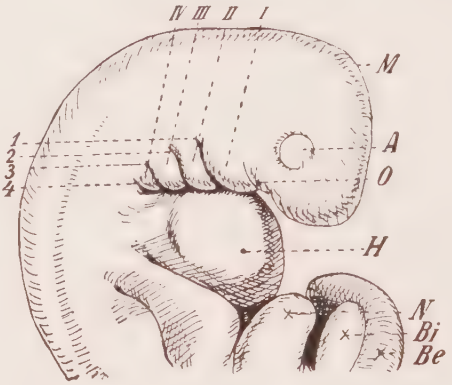



FIG. 160.

FIG. 159.—Embryo 5th week (median longitudinal section); after His. K, upper part of foregut with 4 inner gill clefts; H, brain tube; Ch, chorda; O, upper maxillary process; U, arch of lower jaw; B, bulbus aortae; L, pulmonary groove; A, optic bulb; La, labyrinth vesicle; Sv, sinus venosus; D, Cuvier's duct.

FIG. 160.—Embryo of 4th week (after Rabl); the posterior segment is not drawn. 1, 2, 3, 4, gill clefts; I, II, III, IV, gill arches; M, mesencephalon; A, optic vesicle; O, superior maxillary process; H, cardiac tubercle; N, umbilical cord; B, leg bud; Be, pelvic region.

## Congenital Fistulæ of the Neck, Branchiogenic (Gills) etc., Fistulæ

In early embryonal life four pouches—pharyngeal and inner gill pouches, (endodermal)—are developed between the gill clefts in the lateral pharyngeal walls; from without they are approached by four furrows from the epidermal side—outer gill clefts or pouches (ectodermal)—but no communication is established; indeed, normally they are always separated by a covering. The pouches, but more especially the clefts, soon become more or less narrow channels or tubes (more details by Hammer), and then disappear, with the exception of the first, which participates in the formation of the Eustachian tube, the middle ear, external auditory canal and pinna. (See Kuttner, lit., in reference to the rare kyomandibular fistulae, a lateral cervical fistula communicating with the external auditory canal.) The second pharyngeal pouch forms the receptacle for the pharyngeal tonsil (lympho-epithelial). From the third pouch the thymus is developed in the shape of a long channel, the thymus canal, descending obliquely from the lateral pharyngeal wall to the sternum, where the actual thymus gland develops. The fourth pouch corresponding to the piriform sinus is the anlage of the lateral lobes of the thyroid. This also has a short channel

which disappears early. Parts of these tracts may remain open, according to the prevailing opinion, those connected principally with the second gill clefts, *i.e.*, the cervical pouch (v. Kostanecki), but according to recent investigations (Wenglowski), chiefly those connected with the third gill cleft or pharyngeal pouch (see under thyroid in reference to those which spring from the lateral thyroid anlage). Fistulous channels remain with an external or an internal opening (blind, incomplete, external or internal), or with both external and internal openings (complete). They are called congenital cervical fistulae, gill or cervical gill fistulae, gill cleft fistulae, or simply branchiogenic fistulae.

The outer opening of the fistulae lies in the space between the sternocleidomastoid and the region of the hyoid bone, usually laterally in the neck at the inner margin of the sternocleidomastoid above the sternoclavicular ligament (lateral cervical fistulae), more rarely medially or even presternal (Roth, Chevassu, lit.). The narrow fistula runs obliquely upward, is quite short and has a blind end (blind external fistula); if its outer opening is higher at the anterior margin of the sternocleidomastoid, its course is higher in the direction of the large cornu of the hyoid bone and between the external and internal carotids up to the lateral pharyngeal wall (tonsillar area). In this situation also are the openings of the internal blind fistulae and of the complete cervical fistulae. The internal blind branchial fistulae may dilate within the pharynx (see there) into diverticuli Complete, *i.e.*, penetrating fistulae, can develop only when the covering mentioned above is perforated.

The internal lining of cervical fistulae toward their endodermal side is composed of several layers of ciliated or pavement epithelium (not cornified), under which is a layer of lymphoid tissue; mucous and salivary glands, and muscle tissue (Schlange) are also found. The ectodermal side is composed of layers of cornifying pavement epithelium of the epidermis and accessory glands and hair.

Most of the median cervical fistulae depend on the persistence of the thyroglossal duct. The outer wall of a cystic structure arising from the persistence of a section of the duct, perforates secondarily through the outer skin (see under thyroid). Wenglowski's opinion that rests of the thymus duct may become transformed into a lateral cervical fistula or cyst, is contested by Hammar, since Wenglowski did not take into consideration the fact that the ductus ecto- and endobranchialis, especially the ductus ectobranchialis II (Hammar), participate most frequently in the formation of congenital cervical fistulae.

We are particularly interested in the branchiogenic lateral gill cleft cysts situated deep below the sternocleidomastoid, and in more superficial movable elastic tumors. The development of both is due to incomplete

regression of gill pouches and clefts, and the epithelium which has been preserved, develops into a cyst. The lining varies depending on its endo- or ectodermal origin (comp. Terrier and Lecine), as explained above in reference to fistulae; its contents are accordingly serous or mucous. In the so-called congenital hydrocele of the neck, the contents are often very voluminous. In the branchiogenic dermoid cysts they are composed of a grumous, poultaceous, atheromatous mass. These dermoid cysts occur not only in the neck and presternal regions (comp. Poingt), but also in the floor of the mouth, in the thymus and in the thyroid. If a cyst ruptures through a narrow opening subsequent to accidental inflammatory liquefaction, a secondary fistula appears at once. Since the place of rupture is variable, the position alone is no certain indication of its pathogenesis. A (congenital) fistula may be present before the cyst develops, as the author saw in a 2 year old child, in whom there was present at birth a fistulous opening in the middle of the manubrium sterni lined with pavement epithelium; a cyst the size of a walnut (with ciliated epithelium) began to appear at the end of the first year.

Branchiogenic carcinomas of the neck (Volkmann) are tumors which develop primarily from the epithelial rests of cervical gill clefts, or by secondary carcinomatous metaplasia of the branchial cysts. They occur chiefly in adults, especially males in the forties. They are usually in the lateral aspects of the neck, are covered by the sternocleidomastoid, and soon fuse with the internal jugular vein. They reach the size of a fist, rarely that of a child's head. In a 53 year old man, the author saw a tumor the size of a hen's egg in the trachea and esophagus.

In the differential diagnosis, besides secondary carcinoma of the lymph nodes, *e.g.*, from laryngeal or esophageal carcinoma, malignant tumors of misplaced thyroid tissue (see under goiter) and primary tumors of lymph nodes must be considered; also the rare deep fibromas of the neck (deQuervain), which, as the author saw in an elderly spinster, may become cystic from hemorrhages; the rare lateral lymph cysts (see Jastrov), rare parathyroid polycystomas (Berger), cystic embryomas (lit. by Estor and Massabvan), a case of which was seen by the author (7 months old child, quickly growing tumor, size of a small fist, easily shelled out, operated by Stich), the rare alveolar tumors, some benign, some malignant but not producing metastases, varying in size between a pigeon's egg and a goose egg, and classed by Kohn (see also Neuber, Massaglia) with the so-called paraganglia (see under adrenals) and called intercarotid paraganglion—glandula carotica—intercarotid nodule (Paltauf, Marchand and others, for experimental work in reference to the physiological meaning by Frugoni, Massaglia, Bethke), all must be considered. The latter are located at the bifurcation of the common carotid and consist of groups of cells

bordered by capillaries, some chromaffine, and showing connective tissue septa. The author observed such a case in a 20 year old girl in whom the tumor had fused with the vagus. (This case and a second case in a girl 21 years old was reported by the author and E. Ruppanner under the title: alveolar tumors of the carotid gland (D. z. Chir., 80, 1905) (see lit. in appendix). The single coccygeal gland is of similar structure (coccygeal paraganglion) see v. Hleb-Koszanka.) For a branchiogenic enchondroma,

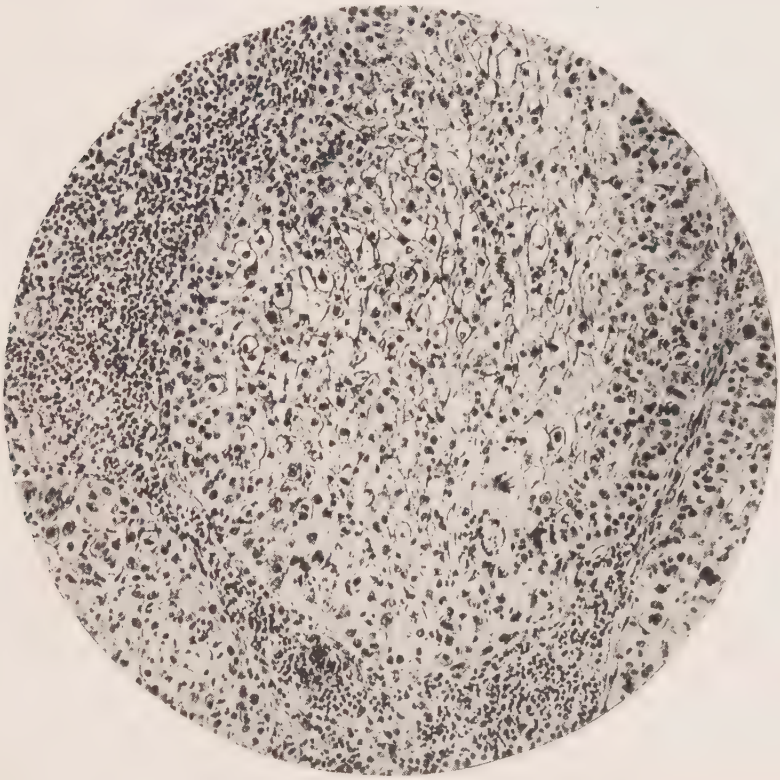


FIG. 161.—Branchiogenic carcinoma. Small tumor present ten years in the right side of neck of man 56 years old. Rapid growth in last six months. Ulceration of skin and neck; extension upwards and downwards. Death from sepsis from ulcerating tumor mass. × 130. L. H. #19855.

see Kolaczek, lit.; for branchiogenic papillary cystadenolymphomas of the paroitid region, see p. 284.

### Inflammations

Inflammations are essentially similar to those in the larynx. In older catarrhs the efferent ducts of the numerous mucous glands are occasionally plugged by glassy masses which project like dewdrops, are symmetrically distributed, and can be wiped away. They must be differentiated from tubercles.

Among others, Askanazy demonstrated catarrh in la grippe, partly, as a catarrh with the formation of pavement epithelium, and partly as a diphtheroid or croupous inflammation.

In pseudomembranous inflammations, the membranes are easily detached because the cylindrical epithelium rests on a basement membrane (see fig. 147, p. 311). Actual diphtheritic involvement is rare. The membranes consist of a laminated, finely fibrinous network containing leucocytes (fig. 162). They often form a tubular cast (fig. 147).

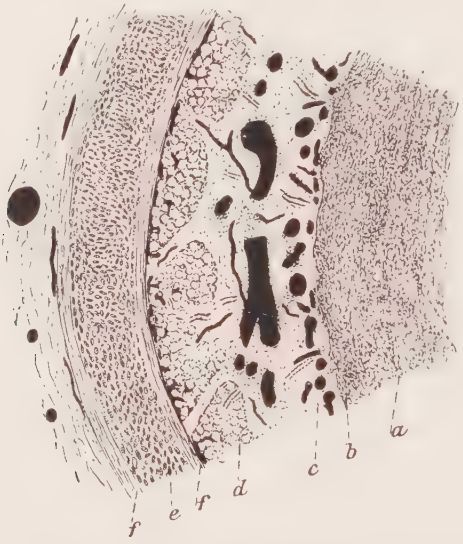



FIG. 162.—Pseudomembranous inflammation of trachea; croupous form, from a child. a, pseudomembrane; b, line on which the epithelium was situated (basement membrane); c, vascular mucosa, vessels injected; d, mucus glands, some excretory ducts in layer c; e, hyalin cartilage; f, perichondrium; (medium magn.).

Sometimes thin pseudomembranes are perforated by sieve-like holes corresponding to the openings of ducts of mucous glands.

Changes in the tracheal mucous glands consist of quantitative and qualitative differences in the mucus produced, and epithelial disintegration as in la grippe, mustard gas poisoning, true diphtheria, small pox, etc.; other substances such as ammonia produce different pictures (see Watjen).

### Specific Processes

**Tuberculous** ulcers are established by the disintegration of subepithelial tubercles in the mucosa, most frequently on the posterior wall, but also laterally and anteriorly. These ulcers, often flat and lenticular, involve the upper, more frequently the lower, and more rarely the middle part of the trachea, while, at the same time, the rest of the mucosa is in a state of active inflammation.

Occasionally, the whole trachea, larynx (often only beginning below the pouches of Morgagni), and the larger bronchi, show innumerable ulcers or give the appearance of a single immense ulcer. There is frequent perichondritis of the tracheal rings (fig. 149), but cicatricial contraction and tracheal stenosis rarely follow. Sometimes curious cartilaginous and bony proliferations result from growth of the perichondrium.

Tuberculosis of the trachea (and bronchi) is only rarely a primary disease (Hedinger, lit.).

**Syphilis** may be primary in the trachea, chiefly in the upper, but more frequently in the lower parts (and of the bifurcation), sometimes in both places. Usually it is accompanied by laryngitis (fig. 163), less often with bronchial syphilis. Syphilitic ulcers starting from flat gummatous infiltrates are the most frequent lesions; they are usually rounded, sharply rimmed, deep and large, often multiple, and occasionally of varying age, with bacony, grumous, smooth, clean, or cicatrized bases. Cartilage necrosis from purulent perichondritis is frequent; as the cartilage shrinks, becomes twisted and is displaced, there is subsequent cicatrization and fusion of one over the other.

FIG. 163.—Syphilitic scars in the trachea shortened to 8 cm., contorted and of unequal widths,—also in larynx. Left margin of epiglottis shows small defect.

The cicatrization is often extensive enough to cause the part or the entire trachea to become markedly distorted, stenosed and sometimes almost occluded to a minute, usually eccentric lumen, or with no lumen. Below the stenosis the lumen is dilated. The trachea shortens and loses its extensibility. Normally the elastic trachea is shortened with expiration, and elongated during inspiration (comp. p. 305). The scars are shiny, satiny, rayed flat spots, or networks like a rope ladder, or like stellate figures, convoluted strands, or rolled up projecting ledges, trabecular bridges or ring-shaped diaphragms.

A tumor-like circumscribed gumma is rare, but more common than the diffuse gumma which is hard in the beginning and later soft and ulcerating.

Sometimes deep extensive crateriform gummatous ulcers cause peritracheal abscesses, purulent suppurative mediastinitis, putrid bronchitis, gangrene of the lung, and rarely erosion of large vessels (cava, innominate, arch of aorta).

The trachea may be compressed from the outside by masses of gummatous peritracheal lymph nodes and its wall may then become secondarily infiltrated and destroyed. Ulcerative, endotracheal syphilis may be present at the same time.

Slighter affections (catarrh, papules, erosions) in the early stage of syphilis correspond to those of the larynx (lit. in reference to tracheal syphilis in the appendix).

Glanders is rare. Scleroma, under nose, p. 300. Small pox similar to that of the larynx (p. 319).

Decubital ulcers in connection with tracheotomy, p. 336.

**Secondary Ulcerations, Erosions, Perforations.**—Malignant tumors of the thyroid, esophagus, aneurysms of the aorta (comp. Hart), suppurations in the vicinity, etc., may rupture into the trachea. Softened lymph nodes lead relatively quickly to perforations, especially in the lower parts of the trachea and the roots of both main bronchi, *e.g.*, anthracotic, and afterwards softened, tracheo-bronchial lymph nodes. Fistulous perforations, or anthracotic scars of fistulae are often encountered, especially at the bifurcation. Perforation of tuberculous lymph nodes is rarer (lit. by Ebert), but may be extensive, and whole caseous nodes gradually crumble, leaving crateriform ulcers or wide open cavities. But this occurs also in anthracosis. Dangerous putrefaction from secondary infection occurs and is followed by necrotic aspiration pneumonia, mediastinitis, rupture into veins and metastases to brain, etc. The cases in which there is perforation both into the trachea and esophagus are the most dangerous (esophageo-tracheal fistula).

### Stenoses and Dilatations

Stenoses may be caused by (*a*) changes within the trachea, such as scars of various origins, pseudomembranes (occasional sudden closure by a folded tubular membrane), granulations at the margin of a tracheal wound, as after tracheotomy, or decubital ulcers; by (*b*) compression from adjacent tissues, *i.e.*, enlarged lymph nodes, mediastinal tumors, especially of the thymus or the esophagus, aneurysms, and particularly goiters (see under thyroid) in which the most severe deformities are seen as shown by Simmonds with plaster casts, by Oppikofer with paraffin casts, etc.

The sabre scabbard trachea also develops without goiter, as in emphysema; it is the most frequent deformity of old age (Simmonds); the cartilages are ossified while in goiter they are soft as usual. See Sgalitzer in reference to the changes in position and form demonstrated in x-ray pictures.

Diffuse dilatations are sometimes observed in senile atrophy. In chronic catarrhs, circumscribed, deep bulgings are occasionally seen (ectasias) or diffuse spindle shaped dilatations, both usually in the membranous part (posterior wall), often with numerous saccular diverticuli between the cartilaginous rings.

Retrotracheal mucous gland cysts of the trachea may be mistaken for diverticuli; they prefer the right edge of the membranous tracheal wall (fig. 164), and force themselves into the loose tissue between the trachea and esophagus. They may be very small to the size of a cherry or walnut. A probe may be inserted into the sac through one or more fine channels corresponding to the ducts. The cyst is filled with viscid mucus or muco—pus, or is lined with trabeculae. Marked connective tissue proliferation may cause the appearance of a firm tumor, a cystoma, filled with channels and cavities (Simmonds, lit.). It is more common in men and is usually combined with emphysema and chronic bronchitis (Maresch, lit.).

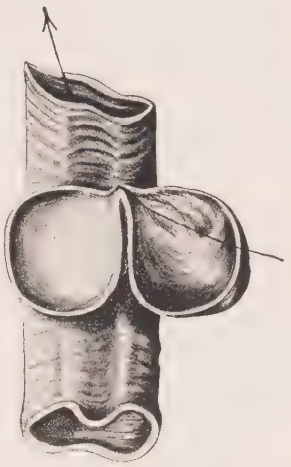


FIG. 164.—Diverticulum-like cyst of mucus gland of trachea. Woman 49 years old, with emphysema, bronchitis, bronchiectasia; 9/10 nat. size.

**Tumors (Lit. in Appendix)**

As a whole they are not frequent. Goiters, usually at the posterior wall, are uncommon, and come by displacement or invasion. They have been known to give rise to a carcinoma (Bircher, lit.). Cystadenomas of the mucous glands, sometimes papillary, are rare (O. Maier). Ecchondroses of the tracheal rings in the form of small coralline nodules, usually multiple, are more common. They may calcify and ossify (osteomas), and are idiopathic, or due to chronic inflammatory changes (lues, tuberculosis, scleroma, Peters). There have also been described similar multiple, idiopathic, fibrocartilaginous enchondromas of the mucosa, not arising from cartilage, but later secondarily related to it (v. Recklinghausen); multiple osteomas may be spread over the whole trachea as pronged ridges and plates (Dennig, Heymann and others). Aschoff, Bruckmann, Schnitzer and others speak of this as osteoplastic tracheopathy and believe that the cartilaginous and osseous masses in the mucosa are the product of an anomaly in the "anlage" of the elastic fibers. On

the other hand, Peters found no connection with elastic fibers (see also Mailer, lit.).

The benign so-called papillomas are unusual (papillary fibro-epitheliomas); they select the bifurcation along with fibromas, lipomas, and adenomas, sometimes multiple and cystic.

Primary carcinoma is exceedingly rare. It is much more common in males. Most cases arise between the 40th and 65th years. It usually begins as a flat infiltration which ulcerates. The author saw such a case in a man 50 years old. In the direction of the adherent apex of the right lung, a cavity had developed almost large enough to admit a hen's egg; there were many infiltrated lymph nodes, broncho-pneumonic foci in both lungs, but only slight symptoms of stenosis and inspiratory stridor; the histology showed cornifying squamous cell carcinoma (see T. D. Bielitz). Papillary, pedunculated and polypoid carcinomas are still rarer. Histologically, the squamous cell carcinoma begins in epithelial metaplasias or congenital squamous cell islands; the cylindrical cell carcinoma is less frequent. In eight personal observations of Eug. Fraenkel (lit.), the medullary forms were in the majority, and frequently were of adenocarcinomatous character. Krompecher describes cylindromatous basal cell carcinomas (see also Ferreira, Marchand), but according to Hamacher, mucous glands should be taken into consideration as starting points, a thought with which Eug. Fraenkel and Langhans are in agreement. Metastases from the latter are relatively rare, possibly first in the regional lymph nodes, rare in the internal organs, but in Eug. Fraenkel's cases they were remarkably frequent. On the whole, they are more frequent than in laryngeal carcinoma. On the other hand, invasion of the adjacent organs is relatively frequent, as is tracheal carcinoma secondary by continuity from carcinomas of the vicinity (thyroid, esophagus). Metastatic carcinoma of the trachea in uterine carcinoma is an exceptional rarity (Doederlein).

Sarcomas, among them the spindle cell variety, are primary in very exceptional cases (Berggren, lit.).

For amyloid tumors, or the so-called tumor-like amyloid, see under larynx (p. 323). For tumor-like forms of lymphogranulomas, see K. Mayer.

## Appendix. Pathological Changes Subsequent to Tracheotomy and Intubation

The healing of tracheotomy wounds by connective tissue is in the form of a delicate linear scar in which cartilage sometimes develops, or by cicatrices with the formation of a cartilage callus produced by the peri-

chondrium (comp. Binder). The cartilage at the cut margins practically never participates in the process.

If the tube is allowed to remain too long, or if the cut was made not exactly in the median line, a pressure necrosis may appear and cause partial sequestration of the cartilage adjacent to the cut. If the tube is once removed and replaced, the wound in the tracheal cartilage heals with more active granulation formation and cicatrization, which enhances the danger of cicatricial stenosis.

Other decubital ulcers appear where a tracheotomy cannula with too much curvature touches the anterior or posterior wall (fig. 278). This also occurs with a well shaped cannula if the incision deviates ever so little from the median line. During intubation, (O'Dwyer), different places may be injured, such as the larynx, especially the pouches of Morgagni and the vocal cords, the lower part of the cricoid cartilage; the upper tracheal rings anteriorly may develop decubital ulcers where the end of the cannula rests on the mucosa. Consequences: cicatricial stenosis or hemorrhage which may be fatal (lit. by v. Bokay, Zuppinger, see also Erkes, Galatti).

FIG. 165.—Polypoid granuloma of trachea after tracheotomy; thick scar in larynx and trachea; sudden death, 3 year old child (thymus 20. 5 gm.); nat. size.

Larger masses of granulation tissue becoming polypoid and as large as a bean can be seen on areas ulcerated by decubitus, or on other irritated areas, thus in the tracheal incision. At times they cause great danger from hemorrhages and suffocation (fig. 165).

Hemorrhages, even swiftly fatal, may result from decubital ulcers. Pressure ulcers of the anterior wall have eroded the innominate artery which, leaving the arch of the aorta, passes obliquely upward and to the right over the trachea. If the edges of the wound become diphtheritic, small branches (of the thyroid artery), but occasionally even larger vessels such as the innominate or the aortic arch, may be eroded (following inferior tracheotomy). (Lit. in reference to fatal secondary hemorrhages after tracheotomy by M. Fischer.)

## BRONCHI

Anatomy of the lungs and the smaller bronchi (that of the larger on p. 305). Two structures are differentiated in the lung: the alveolar or respiratory parenchyma, and the fibrous scaffolding which carries the air, blood and lymph channels and subdivides the lung into lobes and lobules.

They are classified as extrapulmonary and intrapulmonary bronchi the latter into (*a*) extralobular and (*b*) intralobular. The latter, the small bronchi (bronchioles), differ in their structure from the larger branches (comp. p. 305) and are delicate, fibrous-elastic tubules, supplied with a relatively massive annular smooth muscle layer lined with epithelium (end bronchi, respiratory bronchioles), (details by Koike); their walls show hemispherical bulgings—the alveoli.

In the larger bronchi, the epithelium is more stratified; in the medium sized, the lining is simple ciliated epithelium, which becomes polyhedral, small, granular and non-ciliated in the smallest bronchioles.

Every end bronchus divides into two or three wide tubes (alveolar ducts) which are surrounded by alveoli; they separate, and without sharp boundaries pass into the wide alveolar saccules (infundibulae), the walls of which bulge outward in the shape of globular spaces, the alveoli. The wall of the alveolus consists of a connective tissue membrane with abundant elastic fibers. The alveolar duct with the infundibulum forms an empty body in the shape of a bunch of grapes. The alveoli of neighboring infundibuli press against each other and the globular form of the alveoli (the individual grape in the bunch) changes into a polygonal one. Under pathological conditions actual communications may develop between adjacent alveoli (Kohn's pore canaliculi or stomata) fig. 181, p. 393. While v. Hansemann by glue injections thinks he demonstrated these communications in the normal lungs of men and animals, v. Ebner, Miller, Eppinger doubt the preexistence of alveolar pores; lately they have been accepted as normal by R. Marchand and Oertel.

In the fetal lung which develops like an acinar gland, the epithelium of the alveoli is similar in structure to that of the infundibuli, but after the first inspiration, the epithelium is flattened, and the cells are large transparent scales in the adult. Under pathological conditions, such as removal of air from the alveoli (atelectasis), the epithelium recovers approximately its original form, and becomes higher. The alveolar ducts likewise are lined mostly with epithelial scales, but also with polyhedric granular cells in certain areas. The alveolar duct with the alveolus forms an acinus. Others call the respiratory bronchiole with its two or three alveolar ducts, "acinus;" (comp. Loeschke, Husten). Several acini (9 to 15) form a lobule.

The connective tissue scaffolding penetrates from the hilum as septa and divides the lungs into large lobes (right 3, left 2) and these again into lobules. But it also enters the lobules and surrounds the alveolar ducts and alveoli. These septa are consequently called interlobular, interinfundibular, or interalveolar and are in relation with the pleura which surrounds the lung externally. The formation of elastic tissue which begins in the vessels in the third fetal month, follows the bronchi and

pleura; it reaches complete development in the ninth month and grows more quickly after birth (Teuffel; comp. Linser). For more in reference to elastic fibers, see under emphysema.

Lattice fibers are found as a reticulum below the alveolar epithelium (v. Russakoff). For smooth muscle fibers in the interstitial tissue and in the pleura, see Baltisberger.

The bronchial ramifications, and with these the bronchial and pulmonary arteries, also enter the lung by the hilum with the septa. The arteries always lie close to the bronchi in all their ramifications and enter the lobules with them. Within the paths of the septa the pulmonary veins pass from the lung toward its hilum, but their course is entirely different from that of the arteries; they lie along the periphery of the lobules and away from the bronchi as far as possible.

The pulmonary artery ramifies at the level of the alveolar ducts into capillaries surrounding the alveoli like a hair net; although in Cohnheim's sense, it is an end artery, it has some few anastomoses with the bronchial artery. On the pleural surface of the pulmonary saccules the capillaries divide into a wide meshed network with abundant anastomoses from which spring the roots of the pulmonary vein (W. S. Miller). The capillary networks of the different alveoli are in communication with each other. The blood which enters the lung is venous, and gas exchange with the alveolar air takes place through the thin walls of the capillaries and alveoli. Carbon dioxide is given up and oxygen taken in. The pulmonary artery is the functional vessel, and the efferent vessels of the pulmonary vein which carry arterial blood correspond to it.

The two bronchial arteries reach the roots of the lungs from the aorta; they are the nutrient vessels of the bronchi, of the pulmonary artery and of the pulmonary connective tissue. According to Kuttner and others, branches leave at the hilum for the pleura, but Muller says this is incorrect. The pulmonary artery, *i.e.*, the capillaries of the alveolar walls, may be injected from the small bronchial twigs, and thus there must be some anastomoses (comp. collateral distension).

Of the bronchial veins, only those of the larger bronchi carry the blood back to the hilum, emptying it into the azygos or innominate veins. The veins of the smaller bronchi empty into the pulmonary vein and important relations of the small bronchial veins and the pulmonary vein result from this mutual outflow.

If the outflow of blood from the pulmonary vein is impeded, *e.g.*, in mitral stenosis, the bronchial veins become greatly dilated. The veins are never intralobular.

The pulmonary plexus, consisting of branches from the vagus and from the sympathetics, principally follows the bronchi.

Lymph vessels which form a closed canalicular system (Miller) are present in large numbers around the larger bronchi, the lobules and the vessels. They communicate with those of the pleura which have valves, according to Miller, by way of the lymphatics of the pulmonary veins. This is a favorite collecting place for coal pigment in the lymph channels and lymph nodes, which gives the surface of the lung a plainly discernible lobular architecture. Pigment is also abundant microscopically in the arterial lymphatics. In the alveolar walls there are many minute lymph capillaries. See Franke in reference to the course of lymph vessels toward the nodes of the hilum, the lymph channels in the posterior mediastinum, and through the diaphragm into the retroperitoneal tissue behind the pancreas.

Lymphoid tissue is found as minute groups and nodules on the lung surface as well as in interpulmonary situations in the peribronchial tissue (Arnold). There are many more or less rudimentary lymph nodes of variable number and size, but subject to the same changes as the bronchial lymph nodes, *i.e.*, infiltration by dust and invasion by tubercle bacilli (Heller; comp. the experiments of Uffenheimer, nodular lung).

### Inflammation of the Bronchi—Bronchitis

**Acute and Chronic Catarrhal Bronchitis.**—In acute bronchial catarrh, the mucosa is swollen, reddened and covered with more or less "secretion" which contains some desquamated epithelium and leucocytes and sometimes red blood cells. After death, ciliated epithelium exfoliates in masses, due to maceration; otherwise it is found sparsely in sputum.

The characteristics of the "secretion" vary. It may be thick or thin mucus (the latter in bronchitis pituitosa), serous, muco-serous, muco-purulent, purely suppurative. The mucus pours from the active mucous glands; it can be pressed out of them, or is made in the epithelium (goblet cells.) The serous and purulent secretion is a transudate or an inflammatory exudate originating in the vessels of the mucosa.

In suppurative catarrh, the mucosa is always infiltrated by small cells.

According to the condition of the "secretion," it is called simple catarrhal bronchitis, serous bronchitis, muco-purulent bronchitis, hemorrhagic, if blood is mixed with it, purulent bronchitis, broncho-blennorrhea (from mucus, although usually but little mucus is present); this latter frequently becomes chronic.

Chronic catarrhs with little fluid of a viscid mucoid consistency (crachats perles) are called "dry" (catarrhe sec, Caennec). More details by Fr. Muller.

In the adult, acute primary bronchial catarrh is usually confined to parts of the large bronchi and is a mild affection in strong individuals, which passes with the symptoms of so-called cough. The catarrh rarely penetrates into the smaller branches but secondary catarrhs which so often accompany severe infectious diseases are the more frequent causes of capillary bronchitis or bronchiolitis.

Every bronchitis in children or in the aged, whether primary or secondary, shows a tendency to become bronchiolitis, and this becomes of great importance because the inflammation extends to the pulmonary parenchyma (catarrhal broncho-pneumonia) and also because of the easily induced complete obstruction of the small tubules (dyspnea). In the first year of life, acute bronchitis may cause sudden death from suffocation or cardiac paralysis (of medico-legal importance).

In reference to the etiology, see statements under rhinitis (p. 293) and acute laryngeal catarrh (p. 308).

Influenza or la grippe is first a local infection of the air channels, *i.e.*, nose, trachea and especially bronchi.

The important factor is its toxemia, which perhaps attacks most effectively the region of the vagus nucleus (Wiesner), or the vasomotor centre. It can cause death with cyanosis, and acute hemorrhagic edema of the lungs, in spite of all therapy including adrenalin, without the development of severe anatomic changes, such as purulent pneumonia, which is often secondary to invading pyogenic bacteria (comp. under lung). In typical acute cases the secretions of the nose and bronchi, especially the greenish purulent sputum from the bronchial depths, yield the bacilli in pure culture and in immense numbers. The character of the bronchitis is simple catarrhal, or, more frequently, purulent; it is rarely diphtheritic or necrotic. The influenza bacilli, discovered in influenza sputum by Pfeiffer in 1892, are very small, plump, unequally sized, non-motile, gram negative organisms, more difficult to stain than other bacteria with the ordinary anilin dyes. They grow only at higher temperatures, in culture media which contains blood pigment or leucocytes on its surface. For pure cultures, Krause advises the use of agar plates covered with sterile pigeon or rabbit blood thinned out carefully with the platinum loop. After 24 to 28 hours, the colonies are visible as small, glassy droplets. They appear not only in epidemic influenza, but also occasionally in the mouths of healthy people, in lung cavities, etc. (comp. Jochmann, lit.). Recently, a filtrable virus has been suspected of causing epidemic grippe, especially of 1918 (Fejes, Burckhardt, Prell, lit. and others). Many have expressed doubts as to the importance of the bacillus of Pfeiffer (Schottmuller, Graetz, lit.), while others believe they are responsible (Olsen, Neufeld, Messerschmidt-Hundeshagen-Scheer). Fahrig (lit.)

thinks the cause of la grippe is unknown. Absolute proof is still wanting. For the pathology of influenza, see among many others Scheller, lit., Huebschmann, Miboslavich, Prym, Fahrig. [Lucke, B., Wight T., Kime, E., Arch. Int. Med., 24, 154, 1919.—*Translator.*]

In the chronic bronchial catarrh which develops from congestion, emphysema, cardiac affections, (see vena bronchialis, p. 339), vascular and renal diseases, diseases due to dust inhalations, etc., the velvety mucosa is blue or gray blue in color, and the whole bronchial wall undergoes profound changes. Sometimes they are hypertrophic, and the mucosa is markedly infiltrated, thickened, bulging, velvety, granular, sometimes villous and polypoid. Not only is the submucosa involved in this proliferation, but also the deeper layers of the wall. The fibroelastic and muscular strands which lie in bundles in longitudinal, oblique, or circular directions in the wall become thickened into trabecular ridges and projections (trabecular hypertrophy), and the cartilages also may show evidence of hypertrophy, and frequently calcification. In spite of the thickening of the wall, ectasy usually results. The contents of the bronchi are mostly mucopurulent. In other cases there is atrophy.

The cellular infiltrated mucosa changes to fibrous tissue and there is atrophy of mucous glands, of musculature and even of cartilage; the diseased wall, giving way to the air pressure and to stagnant secretions, distends into a thin fibrous membrane. The results of the lighter degrees of atrophy are diffuse cylindrical bronchiectasies. Sometimes hypertrophic and atrophic changes occur in the same individual and saccular hernial ectasies of all layers of the wall bulge into the mucosa. Atrophic and also hypertrophic musculature may show fatty degeneration (Eukushi).

In chronic bronchitis, in acute bronchopneumonia due to measles (McKensie, Ribbert, Weitjen), in dilated bronchi (comp. Schmidtmann), etc., the cylindrical epithelium may be displaced by stratified cuboid or pavement or cornifying epithelium (epithelial metaplasia, comp. Teutschlander). Milky white membranes easily stripped off appear on the dark red mucosa (comp. also Fischer, Kitamura, Haythorn). Confusion with tuberculous bronchitis or peribronchitis has been made in isolated bronchitis, in fibrous obliterating bronchiolitis, and that due to the inhalation of poisonous fumes, such as phosgene (Oberndorfer, W. Koch), acids or dust (of calcium chloride), or the aspiration of coarse foreign bodies (Wegelin), or influenza (Huebschmann), diphtheria, measles (Hart), etc. The author can testify to the destruction of the infiltrated bronchioles, with atrophy of the elastic fibres in measles.

Macroscopically, minute white dots and striae, hard to the touch, can be seen. As the epithelium and part of the mucosa are destroyed, connective tissue proliferation, starting in the wall, spreads to the bronchioles;

their elastic fibres offer but little resistance, and so they tear and shrink (Edens). It may then penetrate the alveolar walls, and even the alveoli (A. Frankel). Lange considers the process an organization of a fibrinous exudate escaping from areas denuded of epithelium, as in cornification of the lung, in which an obliterating bronchitis can be observed microscopically (p. 398) (comp. Galdi, Edens, Hart). Besides the fibrinous exudation, to us it seems essential to have a lesion of the wall sufficiently deep to stimulate an active (reparatory), peribronchial connective tissue proliferation (see Dunin-Karwiska, Vogel).

### Fibrinous Bronchitis

This is also called pseudomembranous or croupous bronchitis. A fibrinous exudate covers the inflamed, infiltrated mucosa where the epithelium has been destroyed, and membranous tubes appear in the larger, and solid casts in the smaller bronchi.

**Development.**—It may be descending from diphtheritic pseudomembranous inflammation of the pharynx, trachea, or it may be primary to infectious or toxic causes. The author will cite two observations in which a fibrinous bronchitis was caused by the inhalation of ammonia, and by aspiration of slaked lime. They did not progress to obliterating bronchitis. In fibrinous pneumonia, casts in the smaller, and sometimes in the larger bronchi of the consolidated area are quite consistently found. They often appear in the sputum. But, as a rule, there is no fibrinous exudation from the wall, the epithelium is preserved, the exudate comes from the infundibuli and alveoli, and congeals in the bronchi. For this reason it is loosely attached; pus cells coming from the wall may cover the cast. In pulmonary phthisis the author has seen the formation and expectoration of casts in branching forms like trees, of whitish yellow color, often containing many tubercle bacilli. Hart saw mucinous casts under similar conditions.

Primary plastic bronchitis (essential), also called "fibro mucous" is rare and its etiology is obscure (Beschorner, Posselt, Fr. Muller, Marchand, Hart, lit.). It may be acute, but is usually chronic and lasts for years. The expectorations contain rolled, branching, ramifying, cloudy, yellowish white casts, not tubular in structure, but filled with air bubbles (fig. 166). They float in water and consist of matted fibrin (Liebermeister, lit.) or more usually of mucin (Grancher, Beschorner, Grandy and others), which led to a comparison with mucous colitis (see under bowel). Cesaris Demel saw pure fibrinous structure in one case which he considered due to compression of the pulmonary hilum by an aneurysm of the arch of the aorta. They also contain red and white and eosinophilic blood corpuscles,

"spirals," and the same crystals which are found in bronchial asthma (fig. 167).

In the differential diagnosis, branching blood coagula must be excluded, as repeatedly found in the sputum in parenchymatous hemorrhages of the lungs. Coagula in pulmonary tuberculosis are less branching and appear only once (comp. Fabian).

FIG. 166.—Branching coagulum; bronchial cast, with essential plastic bronchitis; $\frac{3}{4}$ nat. size.

**Bronchial Asthma.**—In bronchial asthma characterized by sudden attacks of pronounced dyspnea, chiefly expiratory, *i.e.*, air hunger with quick pulmonary distension, Leyden, Ungar, Curschmann and others, found spiral mucous threads of 1–2 cm. in length contained in the glassy, viscid, mucoid plugs in the sputum which is usually expectorated as the attack subsides. Curschmann believed they indicate the characteristics of the disease which he called exudative bonchiolitis, causing a reflex tonic spasm of the musculature of the small bronchi transmitted through the vagus, and thus initiating the attack which may last for hours.

Biermer assumed that this tonic spasm of the bronchial muscles is primary (idiopathic asthmatic bronchitis), but at present it is frequently considered a reflex phenomenon. The primary irritation may come from the bronchi, but also from changes in other organs, such as the nose (catarrhs, odors, hay fever), or the intestinal tract. The spasm is of course combined with swelling and secretion into the lumen (symptomatic asthmatic bronchitis). Others believe that a vasomotor change, consisting of acute dilatation of blood vessels and swelling of the mucosa

with exudation is brought about by reflex processes. According to A. Frankel, (see also Siegel), asthma is a reflex neurosis characterized by typical asthmatic attacks in which three processes are coordinated, *i.e.*, catarrh due to nervous influences (secretory neurosis), fluctuating hyperemia of the mucosa (vasomotor neurosis), and spasm of bronchial muscles (motor neurosis). As to endocrine causes of bronchial asthma, see Hans Curschmann, lit. See Schlecht and Schwenker in reference to points of similarity between bronchial asthma and anaphylactic conditions, and local eosinophilia in the bronchi and lungs in the anaphylactic guinea pig (hypersensitive), also lit. and experiments. See Hans Curschmann in reference to anaphylactic bronchial asthma in skin dyers, and see Besche in reference to so-called horse asthma.

Spirals are found in other pulmonary diseases without asthma such as croupous or bronchopneumonia, fibrinous bronchitis, edema of the lungs, etc. The author has seen them repeatedly (once with asthma) in the viscid, glassy mucus behind a bronchial stenosis due to anthracotic bronchial nodes, malignant tumors of the bronchial wall (primary carcinoma, secondary lymphosarcoma originating in the mediastinum, see p. 278) an endothelioma which started in the pleura (see there), in an invaginated bronchus, etc.

FIG. 167.—Piece of spiral in sputum in bronchial asthma. b, Leyden crystals and leucocytes in sputum in bronchial asthma (unstained).

For the formation of these spirals (lit. by Riehl), which consist chiefly of mucus, the presence of a scanty viscid secretion in the bronchi is required; the forcible respiratory movements develop a pressure, and the accompanying shaking, perhaps even the contraction of the bronchi themselves, combine to twist and push these bodies forward. Thus the central parts of this twisted mucus become so tense that they appear as a homogeneous shining thread, the so-called central thread—but it is not an independent structure—, surrounded by the more loosely arranged spiral mucous envelope. A. Schmidt considers this mucus a special secretion of the minute bronchioles which are devoid of glands. A. Frankel considers it derived from cylindrical epithelium of the finer bronchi; it has undergone mucoid degeneration. Monckeberg, in another theory, believes the mucus is secreted only in bronchi containing mucous glands, and that it enters glandless bronchi by aspiration.

Leyden crystals, as mentioned under fibrinous bronchitis, are also found (fig. 167). They are identical with the colorless Charcot-Neumann

crystals, (H. Kohn points out that the name "Zenker" should be inserted between Charcot and Neumann). They are in the shape of a double pyramid, found in leukemia in all tissues, as in normal bone marrow, in nasal polyps, other tumors, etc. For crystallographic and staining investigations (red with triacid stain), see Cohn and Lewy; for other staining, see Taratynow, (Strauss). Compare the statement of E. Liebreich in reference to Charcot crystals made from any blood, and the relations between eosinophiles and the crystals in blood coagulation. These crystals appear in other pulmonary affections such as emphysema, bronchitis, phthisis, etc., but only rarely. Desquamated bronchial and alveolar epithelium, fat droplets, leucocytes and many eosinophiles are found between the peripheral, loose mucus masses (Fr. Muller and Gollasch). Perhaps the crystals arise from the latter (Naegeli, Marchand), because, according to Kannenberg and Gollasch, they appear and disappear with them, and in the same proportion, although their exact relation is still obscure (B. Lewy). In one of his cases described in detail, Marchand shows his impression of the way these crystals which stain pale red with eosin are formed from eosinophiles—but he was unable to demonstrate direct crystallization from these cells. The blood picture also shows a characteristic eosinophilia, and large numbers of eosinophiles are found in the bronchial secretion; the spirals as such are not considered specific of bronchial asthma, (Predtetschensky); but without eosinophilia, there is no bronchial asthma (Schwarz, lit.). Much is still obscure, but consult the valuable work of Ellis, lit.; Marchand, lit.

The so-called humid asthma is a bronchitis pituitosa (mucous) combined with severe dyspnea.

**Putrid Bronchitis.**—Under the influence of organisms of decomposition the bronchial secretion becomes discolored and acquires its characteristic fetid odor (fetid, gangrenous bronchitis).

The mucosa is coated by a rather firmly attached, grayish yellow layer, or is brownish red, hypertrophic, loose, partly poultaceous, discolored, and covered by a thin purulent secretion usually profuse, and containing friable, cloudy grayish yellow or yellowish brown masses with a sweet putrid odor which are loosely attached in layers to the mucosa. Putrid bronchitis is sometimes localized to isolated bronchi, at other times it is more extensive in both lungs. As a rule, the involved bronchi are markedly dilated.

These friable masses, often over 1 mm. in diameter, soft, and easily crushed (the so-called Dittrich plugs), consist of the fatty debris of epithelium, leucocytes and granule cells, of crystalline decomposition products, and always of many curved needles of fatty acid crystals. On heating on a slide, the crystals melt, forming fat droplets; they dissolve in boiling alcohol and ether.

Large masses of bacteria produce the decomposition. Sometimes there is an admixture of triple phosphates, cholesterin, and leucin and tyrosin. Among the bacteria are long threads similar to the leptothrix; they stain blue with iodine, and often are macroscopically visible in rolled coils. They have been mistaken for elastic fibres. According to Buday, the fusiform bacillus is the most constant and numerous; as a close second, the so-called comma bacillus is present (see under parasites of the oral cavity), and then numerous cocci.

**Etiology.**—Necrotic bronchitis is rarely primary; it may develop from a simple catarrhal bronchitis if the secretion becomes stagnant and putrefactive organisms gain entrance through the respiratory channels. But it is most frequently an accompaniment of ectatic bronchitis in which the conditions favor stagnation. But these same conditions may be present in those phthisical cavities in which the walls are quite smooth and healed; the decomposing secretion floods the bronchi as it is expectorated. Necrotic foci in the lungs are frequent causes of necrotic bronchitis, which may also be present in ulceration of the trachea or bronchi, rupture of an esophageal carcinoma, syphilitic ulcerations in the trachea or the bronchial tree, aspirated foreign bodies, which carry organisms of putrefaction, etc.

**Symptoms.**—Usually the bronchi are diffusely dilated (cylindrical) if the process has lasted for some time, and it may persist for years. The mucosa may be focally destroyed by ulcers. In most cases a severe and generally fatal inflammation of the lung sooner or later sets in, a bronchopneumonia which becomes gangrenous. Usually, anaerobic organisms are found in the oral cavity, bacillus fusiformis, the comma shaped spirillum sputigenum and a form of spirochetae. They cause the actual tissue necrosis (Buday). This is often followed by an infection of the pleura.

Consequences of bronchitis to the bronchial wall, to the vicinity of the bronchus and to the alveolar parenchyma:

Every intensive bronchitis leads to cellular infiltration of the walls accompanied by hyperemia. In the chronic varieties, the walls are fibrosed, thickened and indurated (fig. 169). When the inflammation extends to the vicinity of the bronchus—peribronchitis—there are cellular infiltration of the peribronchial connective tissue and inflammation of the abundant lymphatics—peribronchial lymphangitis—causing their later obliteration by connective tissue (comp. p. 342).

The adjacent alveolar parenchyma may also become involved; inflammatory products appear in the interalveolar septa and exudate in the alveoli surrounding the bronchus. It becomes a peribronchial focal pneumonia (fig. 168).

The inflammation may extend by continuity within the bronchial tube (endobronchitis) to the alveoli. This is the common bronchopneumonia; or the contents of the bronchi are aspirated into the alveoli to produce aspiration bronchopneumonia (aspiration pneumonia).

Blocking of smaller bronchi due to swelling or accumulation of secretion is very frequent. Consequently atelectasis develops in those parts of the lung (see under lung, p. 361). Chronic bronchitis is often followed by emphysema.

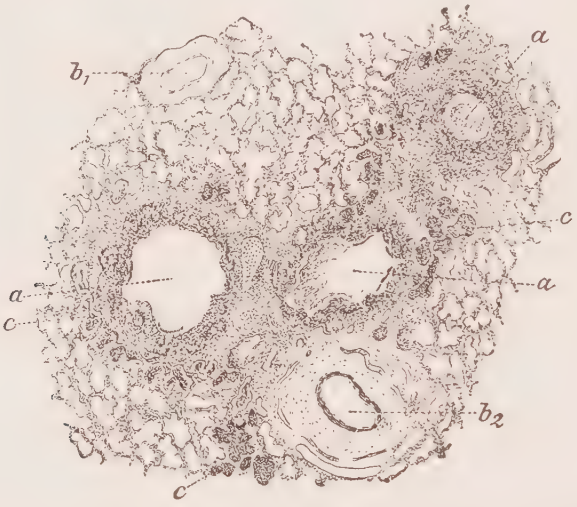



FIG. 168.—Acute bronchitis, peribronchitis and peribronchial pneumonia after scarlet fever; 3 year old child. a, some bronchi filled with fibrino-purulent exudate, fallen out of others; bronchial epithelium partly lifted off, partly visible; $b_1$ and $b_2$, branches of pulmonary artery; c, alveoli filled with fibrinous exudate. Between both larger bronchi a wedge-shaped piece of hyalin cartilage in the cellular infiltrated hyperemic tissue. Alum carmine and picric acid stain; (low power).

### Infectious Granulomas. Specific Inflammations

**Tuberculosis.** Two forms are distinguished: (*a*) Tubercles which on disintegration leave ulcers. The formation of tubercles, chiefly in the larger bronchi, follows caseation necrosis in the lung, (infection by sputum), or more rarely, the rupture of bronchial nodes undergoing caseous tuberculous necrosis. See p. 349 for primary tuberculous bronchitis. For the so-called tuberculous peribronchitis, *i.e.*, tubercles in the vicinity of the smallest bronchi, also called perivascular and peribronchial tuberculosis, see under lung (section, tuberculosis). (*b*) Caseous bronchitis is characterized by diffuse caseation as distinguished from that type characterized by distinct nodules.

It often develops in the smallest bronchioles (fig. 169), and will be discussed in more detail under caseous bronchopneumonia. In larger

bronchi, it is found under conditions similar to (*a*), as well as in bronchiectatic cavities with stagnating contents.

There appears a cellular exudative mass, not characterized by distinct tubercles, mostly caseous, but which may have undergone some fibrous changes. The inflammatory exudate in the bronchial lumen is also caseous and turns into a dry mass non-stainable by nuclear stains. Caseation may involve not only the contents and the walls of the bronchi but also the vicinity, *i.e.*, the peribronchial and adjacent lung tissue (caseous peribronchitis and peribronchial caseous pneumonia). Thus irregular

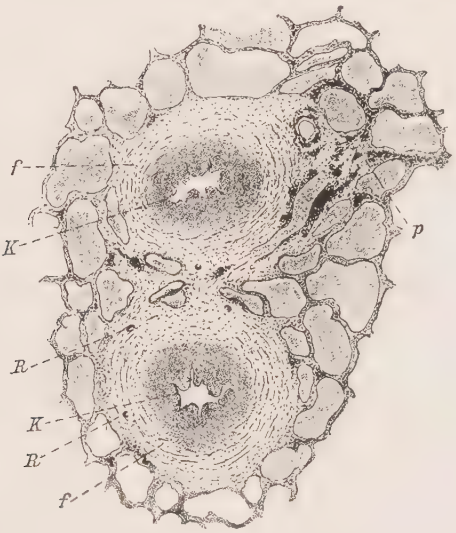



FIG. 169.—Caseous-fibrous bronchitis and peribronchitis. K, caseous material surrounding the irregular bronchial lumen; f, fibrous tissue containing blood vessels, black pigment (p) and giant cells (R). Septa between adjacent alveoli thickened, some pigmented; exudate in alveoli; (low power).

cavities develop, surrounded by caseous material in situations previously occupied by bronchi and lung tissue (fig. 197-c and e). Involvement of blood vessels leads to hemoptysis.

**The Healing Process.**—If the tubercle bacilli die, the process stops. The caseous material hardens and becomes impregnated with lime salts—first like chalk, later more like mortar, or actually like stone, and by indurative fibrous inflammation is encapsulated (fig. 197-d). The whole bronchial wall may undergo fibrous changes and the lumen become obliterated (obliterating fibrous bronchitis). The cavities also heal, *i.e.*, become fibrous and obliterated, or shrink from cicatricial contraction (fig. 197-e).

Tuberculous bronchitis at times is developed before any lesions appear in the lungs themselves, and it may also heal. According to Birch-Hirschfeld, bronchi of the second to fifth order are involved, with predilection for the posterior apical branch of the right lung which cor-

responds to the posterior part of the apex and the adjacent subapical portion. (For anatomy of the bronchial tree, see Narath.) At first an annular tuberculous infiltrate may narrow or occlude the bronchial lumen, the lung tissue collapses, and after obliteration of the bronchi, becomes atrophic, while the focus may heal and become encapsulated. But by disintegration of the infiltrate, the lumen may again become patent, and the tuberculous material carried in both directions. Schmorl demonstrated the frequency of such occurrences; it is said to be correlated to primary stenosis of the thoracic aperture, and kinking of the apical bronchus, *i.e.*, by a subapical pulmonary pressure furrow. For erosion of vessels, see above. The author often saw analogous bronchial findings, likewise multiple cicatricial stenoses, at times a tuberculous, annular stenosing infiltration, or bronchial ulcers. There is often a simple, or a tuberculous caseous bronchiectasis, or possibly merely a cicatricial chalky nodule behind the infiltrate, *i.e.*, the cicatricially obliterated bronchus.

**Syphilis** may lead to ulceration, cicatrization and stenosis (rare). Usually it is confined to the main branches, but may extend to the small bronchioles; these shelving cicatrices have been mistaken for hypertrophic ridges on the inner surface of the bronchi; compare under trachea.

**Glanders,** in the form of small nodules and ulcers, is rare.

### Changes in Bronchial Lumen—Stenosis, Ectasia

**Bronchostenosis.**—Various types are recognized due to the following:

Changes in the bronchial walls. This type is caused by scars from perforation of bronchial nodes, which, overloaded by dust, break down and become sequestrated, from syphilitic scars, from tumors (adenomas, lipomas, sarcomas, and the more frequent carcinomas of the bronchus, tumors of the mediastinum, especially lymphosarcomas, which invade from the hilum, invaginating the bronchi, infiltrating, narrowing and progressing). Inflammatory swelling of the mucosa due to acute or chronic inflammation may cause narrowing or even occlusion of the smaller bronchi.

Occlusion of the lumen from intrabronchial causes such as secretions, pus, pseudomembranes, caseous material, foreign bodies (p. 356), etc., must be considered.

If a fluid inflammatory exudate remains in obstructed bronchi it becomes thickened and caseous so that the bronchial wall surrounds the substance like a sack or capsule. These plugs of secretion may be calcified (bronchial calculi).

Among extrabronchial causes are diseased lymph nodes, chiefly anthracotic, with induration and contraction of the surrounding connective tissue (cicatricial periadenitis, which may also narrow the pulmonary vessels), also caseous tuberculosis and tumors, both mediastinal and pulmonary,

mediastinitis, esophageal carcinomas, and especially aneurysms of the aorta (see p. 141).

The results of bronchostenosis in reference to the alveolar parenchyma vary with the degree. In total closure, the involved lung is completely collapsed; whatever air remains is absorbed by the blood. In incomplete closure, the alveoli dilate to emphysema. The consequences of bronchostenosis in the part of the bronchial tree extending toward the periphery are discussed in the next chapter.

**Bronchiectasis (Dilatation).**—According to the form, we speak of cylindrical or diffuse, and sacculated or circumscribed, bronchiectasia, with the spindle-shaped form between. When several saccular dilata-

FIG. 170.—Cylindrical bronchiectasia, hypertrophic form; surrounding lung tissue, slaty, indurated; 9/10 nat. size.

FIG. 171.—Saccular bronchiectasia. The peripheral end of the distended bronchus is occluded; likewise, a small branch; the surrounding lung tissue has undergone cicatricial changes. 9/10 nat. size.

tions follow each other, they are called varicose bronchiectasis. These several forms may be combined. The alveoli in between are crushed and collapsed, and undergo permanent cicatricial atrophy. From mutual pressure, the walls of touching ectatic bronchi may disappear, and several form a communal sac analogous to anastomosing varices. In rare cases a large cavity takes the place of a large area of lung.

More extensive bronchiectasias are prone to cause cardiac hypertrophy (see fig. 173), and marked cyanosis (drum stick fingers, see under bone).

In diffuse bronchiectasis (fig. 170), the uniform dilatation may extend as far as the pleura. This of course facilitates the exposure of the bronchi during autopsy. Sometimes the most distal ramifications are the ones most markedly dilated. Diffuse dilatations are found most frequently in the lower lobe. When there are saccular or spindle shaped bronchiectases (fig. 171), which at times reach to the pleura, efferent small branches, as

well as the central or peripheral ends, may obliterate (fig. 171). Saccular dilatations are found most frequently in the upper lobe.

**Condition of the Wall.** The walls, especially the mucosa of the dilated bronchi, are either hypertrophic or atrophic, and accordingly, the condition is differentiated into hypertrophic and atrophic bronchiectasis. In the latter, the wall is thinned to a transparent serosa-like membrane; in hypertrophic bronchiectasis the wall is changed as in chronic catarrh (comp. p. 342), *i.e.*, the mucosa is thickened, often polypoid, moist and vascular so that bronchial hemorrhages are frequent (fig. 172).

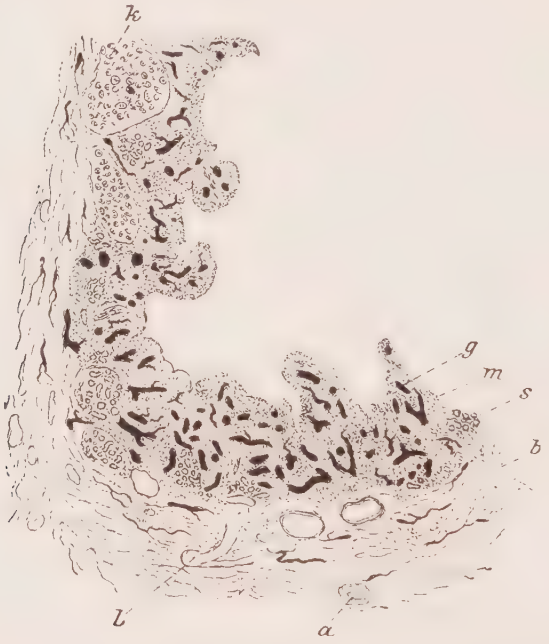



FIG. 172.—Piece of wall of a saccular hypertrophic bronchiectasia. m, mucosa, marked small cell infiltration; here and there polypoid mucosa; many blood vessels (g); numerous mucus glands in the depth s; b, vascular fibrous tissue adjacent to the bronchiectasia (l, longitudinally cut vein) showing here and there small cell infiltration. a, thickened small artery; k, cartilage; (medium magn.).

The epithelium is intact, has undergone mucoid degeneration and desquamation, or is replaced by stratified, low, cuboid non-ciliated or flat cells which give it the appearance of a milky white membrane.

On the inner surface, especially in cylindrical bronchiectases, trabecular hypertrophy, as described on p. 342, is often seen, which determines the lattice-like ribs or shelves running transversely or longitudinally; between the projections which correspond to the strongest places in the wall, the mucosa may bulge out, like a hernia (figs. 170 and 173). In extreme atrophy, the muscle, elastic fibres, mucous glands and even the

cartilage are gradually destroyed and the wall becomes almost completely fibrosed. In a 24 year old man, the author saw spiky rings of bone with marrow cavities.

The walls of saccular bronchiectases are often remarkably thin and smooth like a serosa, and surrounded by abundant fibrous tissue. They may be infected by tubercle bacilli (see p. 348); aneurysms may then appear as in any tuberculous cavity. Rupture of an aneurysm in a non-tuberculous bronchiectasis is rarely fatal from hemorrhage (Chiari).

Bronchiectases contain air and catarrhal secretions which are slimy and thick, or purulent and abundant; if necrosis sets in, putrid bronchitis follows, and may extend to the lung and pleura with a fatal termination. Sometimes the contents thicken to grumous cheesy particles which are later calcified. The masses may be lifted out with the knife. Free concretions are called bronchial calculi. Sometimes the contents are sanguinous from torn vessels, or, more rarely, from ulcerative changes in the walls. For moulds and fungi in bronchiectases, see chapter IX under lung.

### Formation of Ulcers and Bronchiectatic Ulcerative Cavities

The former result from purulent or gangrenous inflammations; ulceration destroys more and more of the mucosa, the wall may be partially perforated or completely destroyed, so that the bronchiectasis is changed into a progressive ulcerating bronchiectatic cavity surrounded by inflammatory peribronchial tissue. These ulcerative bronchiectatic cavities are frequent in pulmonary tuberculosis.

It is not always easy to differentiate between a bronchiectatic ulcerating cavity and an old, smooth, ordinary cavity such as occurs in phthisis (see there), and formed in the softened caseous lung tissue. Proof of its bronchiectatic origin can be supplied by the microscopic finding of tissues from the bronchial wall such as cartilage, glands, smooth muscle, etc.

**The Cause of Bronchiectases.**—They occur in chronic and subacute inflammation of the bronchi, in emphysema, and sometimes in pertussis, measles, etc. These conditions may cause atrophy, yielding, relaxation of the walls and of the tonus, and lowering of the elasticity and contractility of the bronchial wall. The pressure of accumulated secretion helps to dilate the lumen of the bronchi. The development of ectasia is augmented by mechanical causes such as (*a*) increase of intrabronchial air pressure, inspiratory, but particularly expiratory, combined with sudden violent pressure increases, as in violent attacks of coughing with closed glottis, (*b*) the inspiratory pull of the thoracic wall, and (*c*) the elastic pull of the lung. The bronchiectases due to the factors just mentioned are usually cylindrical and often universal.

Peiser thinks there is a possibility of congenital weakness of bronchial walls in the bronchiectases of childhood, especially because this condition may appear in families.

When the bronchi are obstructed or stenosed (see p. 350), secretion collects behind the narrow place, and since there is inflammation of the walls, dilatation occurs quickly, even in a few days, *e.g.*, in diphtheria, with fibrinous casts, and much secretion. Ectasia often develops quickly behind obstructing foreign bodies (beans, etc.) (see p. 356). Vesicular, air-filled bronchiectases have been described by Orth as "tuberculous

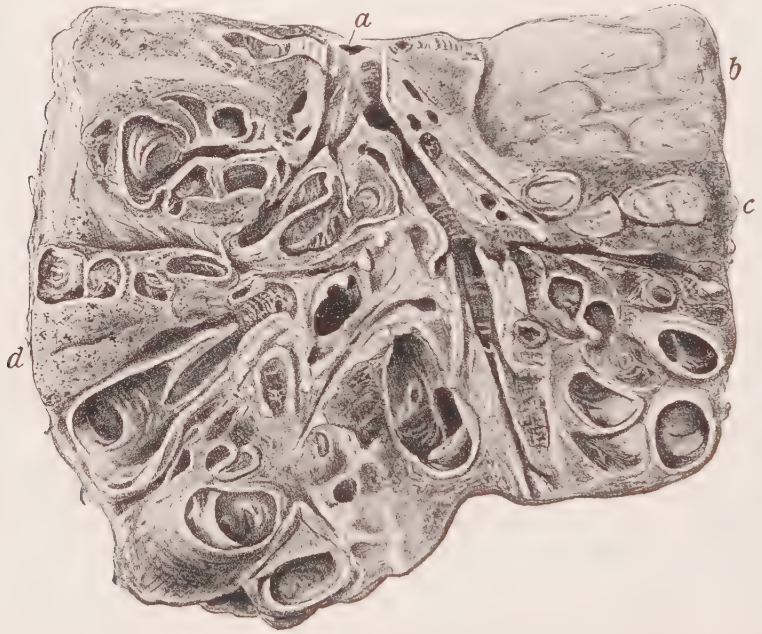



FIG. 173.—Saccular and varicose bronchiectasias in lower lobe (bilateral change). a, wide bronchus with ramifications; anthracotic lymph nodes in neighborhood; b, lung surface with knob-like projections; c, bronchiectasia cut flat; d, cut surface of anthracotic lung tissue. Man 45 years old. Hypertrophy and dilatation of r. ventricle; about ⅓ nat. size.

emphysema;" they were caused by valve-like obstructions in tuberculous bronchitis. See Kirch, lit., in reference to stenosing bronchial tumors.

In cicatricial processes of the lung, "contracted lung," the parenchyma becomes an airless, often cornified tissue, adherent and fixed by the visceral to the costal pleura (adhesive pleuritis). The intrabronchial air pressure is increased as well as the extrabronchial pull, which drags the bronchial walls outward (cirrhotic bronchiectasis). If there are no adhesions of the pleural surfaces, the bronchi within the contracting lung tissue are compressed and become obliterated.

The dilatations are cylindrical if larger areas are affected, and saccular when the contractions of the lung are more circumscribed.

This form of bronchiectasis may involve individual bronchi or those in a whole lobe or a whole lung. The lung itself then becomes a system of cavities which often show the comb-like thickened linings as mentioned (fig. 173). They are separated by thin walls of airless lung tissue undergoing cicatricial changes and grayish black pigmentation.

When a portion of a lung is permanently airless, *e.g.*, when alveoli are atrophic from long exerted pressure of a pleuritic exudate, the bronchi may become dilated, chiefly by inspiratory pressure, since the cushion of air-containing alveoli, which acts as a counter pressure, is absent. (Ectasia due to lack of opposition.)

Dilatation is possible only if the pressure of inspiration is greater than that of the exudate. After removal of the exudate, which, of course, does not permit reopening of alveoli which are atrophied, the conditions are most favorable for the development of bronchiectasis because of the lack of opposing pressure.

A compensatory bronchiectasis in which the alveoli participate, develops, when a portion of a lung atrophies and the remaining, still functioning parts, become dilated (collateral, vicarious, functional bronchiectasis). See lit. in reference to bronchiectasia by Goerdt.

**Atelectatic Bronchiectasis.**—When parts of the alveolar parenchyma are retarded in their development (agnesia), or when well formed alveoli remain airless at birth, or collapse permanently after a temporary expansion with air, the circumscribed airless parts develop into a so-called atelectatic bronchiectasis (Heller, lit. by Edens). The development of the lung, which progresses like a gland shaped like a bunch of grapes, is not carried to its completion. By dichotomous fission, bronchi are formed corresponding to the first developmental stage, but the development of the alveoli, which begins in the 6th month, and which really gives the lung its typical structure, does not take place. During the formation of alveoli, small, thickly grouped sacculations appear as lateral buds from the fine terminal tubules of the bronchial tree, alveolar ducts, and their distal cyst-like distensions.

Atelectatic bronchiectases may show many bulgings and large chambered cavity systems. The cavities are lined with stratified pavement epithelium, or, at times, with ciliated epithelium.

The fibrous dividing walls are often vascular, sometimes delicate, sometimes thick; but most remarkable are the irregular proliferations of the cartilage located in the wall and surrounded by fatty tissue, and the musculature similar to that in muscular cirrhosis (see p. 400). The afferent large bronchi may be occluded or perfectly open. In a case of the first kind, the author found the ectatic bronchi filled with tough, clear, glassy mucus in which numerous spirals were found (see p. 346). If the

afferent bronchi are open, the inspiratory air pressure is of importance in the enlargement of the ectasias.

Atelectatic bronchiectasis is usually in the lower lobe, or, as an accidental rare finding in the upper lobe of individuals of various ages. According to Sauerbruch, 80% of these bronchiectases are congenital, and confined to the left lower lobe. The portions of lung are yellowish white and entirely devoid of pigment, so that they are very striking in appearance and contrast with the acquired forms (see fig. 173); they are usually smaller and firm; the pleura is often thickened and covered with adhesions.

**Fetal Bronchiectasis (Congenital Cyst Formation of the Lung).**—In rare cases, as first described by Meyer and Grawitz, diffuse, spreading, bronchiectases develop in the fetus (see Hondo and lit. by Peiser). Grawitz demonstrated ciliated epithelium. The author has mentioned two observations of this kind. In one, the lung of the fetus, 42 cm. long, was changed into a spongy tissue of cystic or emphysematous appearance (honeycomb lung); the right was small and firm (comp. also Box and Peiser Pappenheimer, lit., Hueter, Buchmann). In the other case (35 cm. long fetus), the right lung was small, but the left was remarkably enlarged (length 5.5 cm., right 2.5 cm.) and distended. On section, the lung had a meshed appearance; large smooth branching cavities occupied the place of the parenchyma. There were connections between the bulgings and cavities and the open main bronchus. In other cases (rarer), both lungs are involved; if only a part of a lobe is changed it may be surrounded by thickened lung tissue like a cap; occasionally it becomes pedunculated or even separated. To explain these peculiar changes, we must consider malformations and impeded development (agenesia), which permit the development of larger bronchi, but not of alveoli. In other cases, it is assumed that retention of secretion behind inflamed bronchial stenoses caused dilatation. Virchow and Klebs thought of dilatation of lymphatics. Orth speaks of congenital emphysema in a 4 year old child, which he compares with the case of Klebs; O. Stoerk considers some "vesicular malformations of the lung" as neoplasias, a "cystic, fetal bronchial adenoma," (comp. also Wechsberg); Lohlein, in reference to a cystic papillary lung tumor (69 year old man), thinks of the possible end result of a fetal bronchiectasis (lit. by Schneider, see also A. M. Peppenheimer).

### Foreign Bodies

Foreign bodies enter the right bronchus more frequently than the left since the right bronchus is shorter, wider, more perpendicular and more the direct prolongation of the trachea. For length of trachea, see p. 305. The bifurcation lies at the level of the fourth to fifth thoracic vertebrae.

If the foreign bodies are hard or pointed, they may become firmly wedged or impacted in the tissue; decubitus and ulceration follow according to the character of the bacterial or chemical contaminations attached to the foreign body. Productive inflammation, suppuration or gangrene of the underlying bronchial wall, the peribronchial tissue and also sometimes of the adjacent lung parenchyma and pleura are consequences. In the bronchi themselves, an extension of purulent or necrotizing inflammation takes place, so that behind the firmly wedged foreign body a pronounced bronchiectasis develops in a short time. Productive interstitial pulmonary changes develop when the foreign body is present for longer times.

A bean had lodged in the right main bronchus of a child, and the author saw the right lung riddled by cylindrical and saccular, pus-filled bronchiectases, while the intermediate parts of the lung tissue were airless and had undergone grayish yellow hepatization. The process developed in a few weeks.

In reference to foreign bodies in the bronchi, see Hofmann, Konjetzny, lit., Toyofuku, Bayer, Kofler, Brunings and Albrecht, lit. and others.

**Translator's Remarks.**—The term "arachidic bronchitis" is given to that due to the presence of a peanut kernel (arachis hypogea) in a bronchus, because of the particularly violent reaction to the presence of this body. Later experience has shown that other vegetable substances cause the same changes in contrast to the absence of reaction around metallic bodies. See Jackson, C. and his coworkers, *e.g.*, Atlantic Med. J., 28, 506, 1925 and Surg., Gyn. & Obst., 42: 305; 1926. Bronchoscopy and Esophagoscopy, Saunders, Phila., 1922. See also "Live fishes in Food and Air Passages of Man," Gudger, E. W., Arch. Path. & Lab. Med., 1926, 2, 355.

Inhaled dust can always be found in bronchi and lungs; if very abundant it causes irritation (see under pneumokoniosis).

Foreign bodies may enter the bronchi through perforations from the vicinity, to be aspirated into the lung, or to be coughed out.

This may be blood from aneurysms or ulcerating tumors; pus or purulent necrotic masses from perforated abscesses or necrotic foci in the lung, mediastinum or softened bronchial lymph nodes; caseous or calcareous products or sequestrated debris of caseous or suppurated bronchial lymph nodes (comp. Paunz). The fragments reach the trachea and larynx from the bronchi and may be coughed up, or become wedged in the rima glottidis and cause suffocation. Tuberculous material may also be aspi-

rated into the lungs and cause extensive secondary foci, especially in children. Osseous fragments of ossified lymph nodes have been found.

Tumor masses from ulcerated tumors, especially carcinoma of the esophagus, food particles, through a perforated esophagus, echinococcus cysts by perforation of a liver cyst into the lung, or by rupture of an echinococcus sac (rare) formed in the lung itself, have all entered the bronchi.

### Bronchial Calculi

Calculi have been found as large or larger than cherry stones and composed of thickened exudates impregnated by lime salts. They are found most frequently in saccular bronchiectases. In addition to bronchial calculi, better called broncho-pulmonary calculi, stony concretions have also been found originating in the lungs from calcification of caseous foci, or more rarely from fibrous scar tissue, or in the tracheo-bronchial nodes (comp. above) which may have reached the respiratory tract.

### Bronchial Tumors (see under Lung)

**Traumata.**—See Schonberg in reference to rupture of bronchi from compression of the thorax.

(Anatomy on pp. 338 and 339.)

## LUNGS

### Post Mortem Changes

The most important is the acid post mortem softening or pneumomalacia acida (cadaveric), see under stomach. Gastric juice enters the pharynx from a relaxed esophagus, and from there gains entrance into the respiratory channels, when pressure from abdominal gases, the position of the body or artificial respiration on the cadaver make the escape of stomach contents possible; or, doubtless in many instances, gastric juice is aspirated into the respiratory tract during agony (Deneke and Nassau), or it enters directly after the wall of the stomach, diaphragm and pleura are eroded by the gastric juice. It is usually the left lung that is digested. By virtue of its digestive action, the gastric juice produces cavities and softened areas, or perhaps only spotted infiltrations. The acid foci are usually darker than other places. The posterior and lower parts are especially often and intensively digested because of settling of the gastric juice in these regions (hypostasis of the blood).

The absence of any inflammatory changes, the acid reaction, the microscopic finding of food remnants prevent this condition from being mistaken for necrotic foci. For putrefactive emphysema, see pp. 338 and 339.

### Malformations

(Lit. by Schneider, and in appendix.)

They play an unimportant part in pathology. Lobar abnormalities are relatively frequent; the right lung may have two or four or more lobes, the left three lobes. In almost one-half of all lungs encountered, there is a small accessory lower lobe. Intrathoracic accessory lungs, also infra-diaphragmatic accessory lungs—abdominal lungs—have been described at times. In situs inversus, the right lung has two—the left lung three lobes. If a lobe is undeveloped, or incompletely developed, the other undergoes compensatory hypertrophy and fills its side of the thorax, often with astonishing changes in shape. Bilateral pulmonary hypoplasia is rare (Glinski). For congenital bronchiectasia, see p. 356. See Urbach, lit., in reference to rare congenital pulmonary hernias due to defects of the bony, cartilaginous or muscular parts of the thoracic wall. Some are also traumatic, while others are acquired spontaneously. Malformations of the lung are often combined with congenital diaphragmatic hernias.

### Simple Changes of the Air Content

Normal air-containing lung tissue is soft, compressible, and crackling. The lung of the newborn is filled with air, first in the apices and then in the peripheral parts when it becomes light red from the mixture of the red color of blood and the white color of finely distributed air (see Tendeloo).

**Atelectasis and Collapse.**—In atelectasis, the alveoli of a portion of a lung contain no air, they lose their polygonal shape, and the walls touch each other. This condition is also known as collapse (imperfect distension). The latter term presupposes that the alveoli previously contained air and collapsed afterward.

In collapse, however, the air does not necessarily disappear completely, a condition to which the term complete collapse is applied. As far as absence of air is concerned, it is equivalent to atelectasis, and it may, for instance, be said that gas pressure in the pleural cavity (in pneumothorax) causes complete collapse, leading to atelectasis.

Complete collapse can be seen in acquired atelectasis due to absorption of air from the alveoli (active), the afferent bronchus of which is occluded, or in absence of air caused by surface compression, when the alveoli are emptied by outside pressure (passive).

The term is also used when the lung of a cadaver is exposed to the atmospheric pressure on opening the thorax. The lungs then collapse but not completely, and less so, if the elastic retractive power has been impaired (comp. red induration, emphysema). This retractive power is much greater during life than after death.

In congenital atelectasis, the fetal absence of air persists. If the lung of the newborn does not expand (fetal atelectasis, atelectasis in a narrower sense), it remains small, bluish red, of flabby, glandular consistency some what like a flabby pancreas and it does not crackle on pressure. On section, it is a uniform brownish red which must not be mistaken for the color of pneumonia, which may of course occur in the newborn. In contrast to a lung which has respired, it does not float. Often, unimportant mucous plugs or possibly bits of meconium which were aspirated from the amniotic fluid, prevent the air from entering a lung; histological investigation must not be forgotten (embedding) (comp. Thomas, Strassmann, lit.). In other cases, more serious reasons are present, *e.g.*, in the respiratory center (cerebral compression from intracranial hemorrhage after the use of forceps). Partial atelectases can be recognized after opening the thorax as darker, sunken, airless regions which may be blown up by way of the bronchus. See Peiser in reference to other findings after previous injection with formalin, *i.e.*, embalming. The floating test (trachea is ligated and the lungs lifted out in toto) is of medico-legal importance, but the value of this so-called "life test" is diminished for several reasons. The atelectatic lung may float from gas formation due to anaerobes which enter the fetus from a corresponding infection of the uterus (uterine tympany), (Hitschmann and Lindenthal). This is never due to cadaveric decomposition alone, as was formerly supposed (Bordas and Descoust; comp. Ungar, lit.), or rarely (Harbitz, Ruhs) (comp. decomposition emphysema, p. 363). At any rate, if a decomposing lung floats, it does not prove that the child has breathed, (comp. Molitoris). Atelectasis can be found in children of weak vitality, *i.e.*, in those which die early, and which demonstrably have lived for some time, even days, and which have cried, therefore actually respired. The lungs gradually lose their air as respiration progressively weakens, and a certain degree of collapse develops because smaller bronchi are occluded by mucus and the alveolar air is absorbed even to the stage of total atelectasis (Ungar). Breathing then ceases (asphyxia), followed by cessation of circulation (lit. by Kathe, Marx). Lungs which were filled prematurely in the uterus contain considerable vernix inspired with the amniotic liquid and may be air-containing and therefore float, owing to the light specific gravity of the vernix (Ahlfeld). In rare cases, the lungs of still born children may contain some air due to premature intrauterine respiratory movements, or due to a spontaneous inflow of air after rupture of the fetal membranes, or after manual or instrumental procedures. Blowing in of air, or Schultze's method of artificial respiration may also unfold the lungs to a greater or less degree of inflation (comp. Schonberg, Strassmann, Hofmeier). If the respiratory tract (and the stomach) of the newborn

with atelectatic lungs contain meconium, most probably the child was suffocated; during suffocation it passed meconium prematurely into the amniotic fluid and aspirated the mixture (see details in reference to meconium under intestines). In doubtful cases, the lung test is supported by the gastrointestinal test (Breslau) which latter, by itself, is of no value (comp. Ungar). As is well known, the swallowing and sucking in of air makes the whole digestive tract contain air (12–24 hours). If the air is in the upper parts of the gastrointestinal tract, it suggests life of only a few hours' duration, if the whole tract is filled, it points to life of at least one day's duration. If decomposition has occurred in the bowel, the test has no value. See under kidneys for uric acid infarcts in the newborn.

**Compression atelectasis** (also called passive collapse) usually involves only part of a lung and is caused by:

1. Narrowing of the pleural cavity by transudates, exudates or air (pneumothorax). Fluid usually empties the lower parts of air, since no inspired air can enter, and the reserve and residual air are pressed out of the alveoli. According to some, this type of atelectasis is, as a rule, the effect of simple retraction, since the pressure of an exudate is usually not as high as atmospheric pressure (comp. Bruns).

2. Space reducing conditions in the thorax such as tumors, aneurysms, cardiac hypertrophy.

3. Decrease of space by marked change in the shape of the thorax, especially in rachitic kyphoscoliosis. The hypertrophy of the right ventricle, following the compression, diminishes still more the space available for the lungs.

4. Compression due to high position of the diaphragm as in ascites, meteorism, tumors (see fig. under ovarian cyst), echinococci of the liver or spleen, etc., diminishes the size and blood content of the lungs; their color is light or dark brown, gray or slaty; they are pliable without crepitating, of flabby elastic consistency, such as that of a moist piece of leather. On section, the tissue is even more dark; if coal pigment is abundant, it is black and remarkably dry. Small pieces placed in water expand very quickly.

**Absorption atelectasis,** or true active collapse (fig. 186) develops:

1. From swelling of the mucosa in bronchitis (especially in early childhood) causing the occlusion of a bronchus. This is called obstructive atelectasis, or lobular, passive collapse of the lung. No fresh air passes into the pulmonary parenchyma, beyond the obstruction. The air already present is absorbed by the blood, first the oxygen, then the carbon dioxide, and finally the nitrogen (Lichtheim). In this way the pressure disappears which the alveoli exert on the enmeshing capillary network like an air cushion. The capillary pressure is increased and the capillaries are

filled to excess, become convoluted and hyperemia results. Since the capillary blood is not oxygenated, it retains its venous color. The alveolar walls approach each other and finally touch. For details in reference to the circulation of the blood, see Bruns.

2. Quickly occurring paralysis of the respiratory muscles (diaphragm, intercostals) may cause active collapse of a whole lobe (massive pulmonary collapse, Pasteur).

The atelectatic hyperemic areas, as a rule, lobular, are deep bluish red and sunken to a lower level than the air containing adjacent parts from which they are sharply demarkated; they are of flabby, moist consistency, especially if larger parts of a lobe are involved. On section the airless regions due to collapse are also more moist, and more venous in color than the tissue from which the air has been pressed.

The collapsed areas which have become airless by absorption are in the same condition as those in compression atelectasis, but, as a rule, in collapse there are inflammatory complications present such as bronchopneumonia due to the primary changes (bronchitis).

**Further changes in the atelectatic, or collapsed areas.**

(*a*) **Splenization** (atelectatic hyperemia plus edema). Ordinarily some fluid exudes from the capillaries into the alveoli and is expired as water. If the bronchus is blocked, the fluid collects in the airless alveoli (edema) and redistends them. The collecting of fluid is made easier because counter pressure is absent in the alveoli. The edematous fluid and the atelectatic hyperemia give the lung tissue a spleen-like appearance.

When bronchopneumonia is added the fluid becomes cloudy and cellular. Edematous, non-hyperemic, atelectatic tissue is gray, glassy and gelatinous.

(*b*) Atrophy of atelectatic lung tissue, so-called collapse induration. Re-distension by the insufflation of air is possible if an atelectasis is of short duration and the collapsed alveolar walls separate, but if the condition has been present for some time, the epithelium is desquamated and the denuded walls adhere and fuse to each other. The alveoli become atrophic, the interstitial tissue proliferates until cicatricial induration renders the pulmonary architecture unrecognizable. If the focus is subpleural, the pleura also proliferates. For atelectatic bronchiectasis, see page 355.

**Translator's Remarks.**—Pulmonary collapse is met post operatively over larger or smaller areas, possibly due to obstruction by mucus of smaller bronchi or to paralysis of the diaphragm, etc. It must not be mistaken for the bronchopneumonia following anesthesia. In many cases it is accompanied by edema. At autopsy, however, active bronchopneumonic patches are usually discovered. See Leopold, S. S., Am. J. Med. Sci., 167, 421, 1924.

### Emphysema (to Blow Up)

This, in contrast to atelectasis, is a condition due to an increase of air. Several forms are distinguished.

**Short Resumé of the Various Forms of Emphysema.**—In distension of the lung, alveolar ectasia, or acute vesicular emphysema, the infundibuli and alveoli are acutely distended with air, perhaps to their maximum capacity.

In chronic vesicular or true emphysema, the infundibuli and alveoli are overfilled with air, and since the walls are fragile they are stretched more and more; tearing and atrophy take place making larger empty spaces which are not simply overdistended infundibuli or alveoli, but vesicular air spaces formed by confluence. There should be differentiated: (*a*) the essential universal emphysema, also called chronic idiopathic or hypertrophic emphysema due to weakening of the elasticity of the lungs depending on congenital weakness of the pulmonary elastic tissue, or on a chronic bronchitis, or on continued forced expiration (wearing out); (*b*) the so-called vicarious or secondary emphysema is an overdistension of air-containing parts subsequent to atrophy and functional removal of parts of the respiratory surface; (*c*) senile emphysema, also called atrophic, due to senile weakness, atrophy and fragility of the fibrous and elastic elements (also smooth musculature?) of the infundibular and alveolar walls.

In interstitial emphysema, or traumatic emphysema, the alveoli are torn by acute overdistension or acute injury. The air penetrates the interstitial tissue, under the pleura and further.

In putrefactive emphysema, gas bubbles of decomposition fill the tissues. It is occasionally seen during life in putrid decomposition of tissue (gangrene). In interstitial decomposition emphysema, the gases are contained in the interstices of interstitial (interlobular) connective tissue, in the subpleura as vesicles, and in the blood vessels (comp. statements of Balthazard and Lebrun, Ruhs, decomposition bubbles in the lung of the newborn; also see p. 360). Occasionally this enables an atelectatic lung of a stillborn to float; the fetal blood contains gas forming bacteria and gas bubbles penetrate the connective tissue septa. A pneumonic lung which sinks in water may float after decomposition is advanced (comp. Olivecrona).

**Pulmonary Distension.**—Increased inspiratory efforts cause acute distension of the infundibuli and alveoli in parts, or in entire lungs (acute vesicular emphysema). If an entire lung is acutely distended it reaches its maximum size and looks like a balloon. In contrast to chronic emphysema, there are no changes in the lung substance; if the organ is carefully squeezed, normal lung tissue remains. Since the vessels are markedly

compressed between the greatly distended spaces, the color of the distended parts is pale. In chronic emphysema, the vessels also are atrophic.

Causative Conditions. Acute distension, also called emphysema aquosum, or better, dry pulmonary distension (Strassmann), is sometimes seen in the lungs of the drowned, but only if the drowning individual sank after deepest inspiration; the quantity of air may exceed the common amount by 2 to 3.5 liters. The supposition is that the water sucked into the bronchioles prevents the air, which is carried in before the water, from escaping, and subjects it to high pressure until it can again expand when the thorax is opened at autopsy. If the amount of air present is less before sinking, only parts of the lung, especially the free borders of the anterior and upper sections show dry distension; the other parts are saturated with aspirated foamy fluid (comp. ref. of P. Fraenkel, and p. 413). During suffocation also, acute distension may occur from forced inspiration, as well as when bronchi are partly occluded by a valve-like mechanism by which inspiratory air may enter, but expiratory air cannot escape. Such conditions are found in spasm of the musculature of the small bronchi in asthma, but more frequently in the presence of pseudomembranes, or even simple acute bronchitis (distension bronchitis), which usually, although not necessarily, is accompanied by violent cough, especially in children, in whom it is often combined with partial atelectasis and focal bronchopneumonia (fig. 186) (comp. Tendeloo). Wassermann described pulmonary distension in extensive influenza pneumonia.

**Chronic Vesicular True Emphysema.**— In contrast to pulmonary distension, there is a permanent change in the lung tissue. As the spaces are more and more distended by air, the otherwise normal alveolar passages and alveoli (as in distension) are ruptured and wide air spaces form by atrophy of dividing walls. The gaps enlarge and coalesce more and more. Finally there appear large spaces including the vesicular distended alveolar duct into which remains of the septa jut like spurs (fig. 174-v). As the distension increases, the atrophy involves the elastic fibers, the capillaries, and smaller blood vessels; even the coal pigment disappears, so that hollow spaces the size of peas, cherry stones, hen's eggs, or even that of a child's head, air filled, clear and transparent, are lifted above the lung surface (bullous emphysema).

Rupture of these surface bubbles may cause fatal pneumothorax, unilateral, or bilateral (comp. Massini and Schoenberg; lit. by Faschingbauer).

Within the larger cavities, there remain branching scaffoldings or perhaps only remnants of the larger vessels and bronchi.

To differentiate between bullous emphysema and bronchiectasis, see page 351 and note that in the latter, the contents consist of secretions

and concretions, and in pure emphysema of air, if pneumonia has not been added to the emphysema.

Two opinions are expressed in reference to the process by which the abnormally wide communications are produced between the alveoli. According to Ribbert, v. Hansemann-Sudsuki, the pores distend into larger round or oval holes (see page 338), but Eppinger, who does not believe Cohnheim's pore canaliculi are present in normal lungs, explains the process as one caused by perforation, or by splitting of the elastic tissue due to pressure atrophy. The pictures interpreted as dilated pores can easily be seen on lateral aspects of alveolar walls in the early stages of emphysema, *i.e.*, we can see round or oval gaps sharply outlined. But

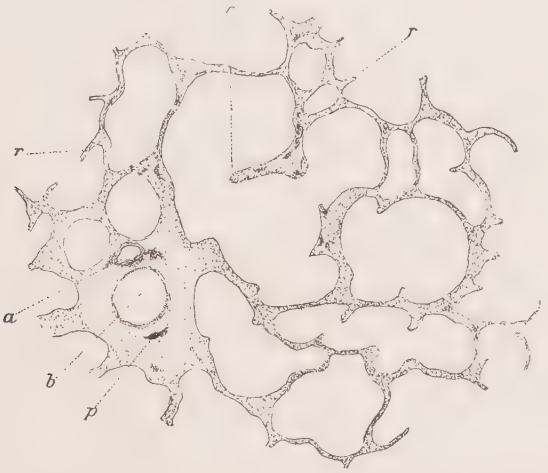



FIG. 174.—Chronic emphysema of lung; a, pulmon. artery; b, bronchus; p, coal pigment; r remains of alveolar septa; (low power).

besides these, there are other quite irregular, large, ragged spaces differing from simple emphysema; at least they might be pores torn from increasing ectasia, although their irregular outlines and large numbers correspond more to atrophic pressure disappearance, to which all elements of the wall succumb (coarser and finer intercapillary elastic fibers, connective tissue fibers, capillaries, epithelium; comp. Orsos, and later Loeschke).

Usually the change begins along the anterior upper margins, especially the lingula, *i.e.*, in places which on account of topographic position are least protected from dilatation by outer counterpressure; from there it gradually spreads downward and posteriorly.

The central and paravertebral parts may remain free of changes.

Emphysematous tissue which has lost its elasticity does not contract when the thorax is opened. Atrophic emphysema, however, is an exception.

The alveolar epithelium often undergoes fatty degeneration; the bronchial musculature is sometimes hypertrophic, but in older cases usually atrophic; at all events, the bronchi dilate. The lymphatics in the interstitial tissue between the air spaces are partly atrophied as are the capillaries and later the larger blood vessels also, in which thromboses and obliteration due to organization of thrombi are common. Emphysematous parts lose their pigment (comp. Grawitz) chiefly because, according to Ohkubo, the pigment enters the thinned veins.

Sudsuki could find no marked morphologic changes in the elastic fibers to explain the beginning of emphysema; indeed, the smallest fibers were sometimes increased, as a regenerative new formation, according to Orsos, but Eppinger believes the beginning of emphysema is found in the disappearance of the finest elastic fibers where the wall has been split. Later, the coarser elastic fibers are forced apart, become narrower, are torn, and are relatively few in number as can easily be demonstrated by elastin stains. Russakoff noticed thinning of the lattice fibers. Tendeloo doubts the existence of anatomic changes which might be the cause of the loss of elasticity in the emphysematous lung, and considers the anatomical changes in the elastic fibers not primary, but secondary, due to the stretching, just as in the similar so-called vicarious emphysema. Besides this, in chronic idiopathic emphysema, there are parts showing new tissue formation among the coarser elastic fibers of the meshed alveolar scaffolding, as well as the fine intercapillary elastic reticulum and in the corresponding collagenous fiber system (simple connective tissue) (see Orsos). In spite of the distension of the lung, the respiratory parenchyma is reduced in surface area (dyspnea). The circulatory disturbance consists of uneven blood distribution within the lung, which, on the one hand, causes hyperemia of the parts to which the blood can gain access, especially the bronchial mucosa which is the seat of a catarrh, and, on the other hand, stasis in the pulmonary artery, a disturbance which may be compensated for some time by hypertrophy of the right ventricle. Hoffmann also believes the impaired suction power of the lungs is a factor which makes the work of the heart more difficult (see Einhorn). If compensation fails, severe obstructive symptoms appear ending finally in cardiac death.

There are three forms of chronic emphysema:

(*a*) In essential universal emphysema, also called chronic idiopathic (true) emphysema, the macroscopic appearance of the lungs is very characteristic. The most pronounced cases are indeed often seen in individuals in their best years. Externally, the shape of the chest is striking, consisting of a barrel-like dilatation of the thorax which is fixed as though permanently in the inspiratory position, often concomitant with hypertrophy of the respiratory muscles such as the sternocleidomastoids, scaleni,

trapezius. The diaphragm is in the fifth to sixth intercostal space and the heart is pushed downward. When the thorax is opened, the distended lungs do not retract because of loss of their elasticity, but remain in inspiratory distension. If the edges also are emphysematous, the pale surface is

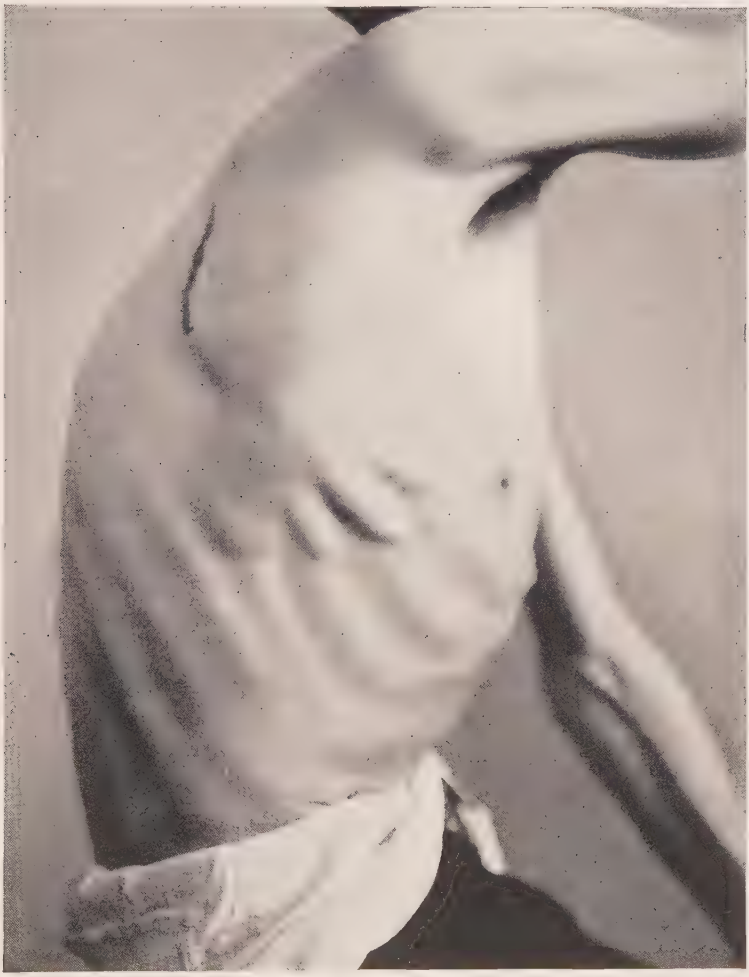


FIG. 175.—The barrel shaped chest of emphysema. A man 40 years old who complained of asthma for many years. There was a difference of only one inch between inspiration and expiration as measured by a tape under the axillae. At this stage he was unable to work on account of the dyspnoea. His heart was markedly enlarged and probably somewhat dilated although there was no edema present. There was slight kyphoscoliosis of the vertebral column. According to his history this had been developing over a period of twenty years. L. H.

rounded and smooth, but sometimes bosses of emphysema bulge on the surface, usually most pronounced at the apices, bases and sharp edges. The organ is light in weight and may be translucent if held against the light. It feels like a feather pillow, without elasticity, and finger impres-

sions remain. It cannot be much enlarged by inflation. The large bronchi are usually more or less dilated.

Pulmonary hernias are rare, but occasionally a part of the lung is forced under the skin, through a tear in the intercostal musculature; (lit. by Urbach).

Causes of Essential Emphysema. In reference to the physical causes, it is assumed that the increased inspiratory pressure, as well as repeated increases of the positive expiratory pressure when there is an impediment to the free exit of air, are factors. Ribbert assumes that the small bronchi are compressed by the distended air spaces. But to this must be added as an essential predisposing factor a diminished elasticity of the lungs, partly congenital (see Bauer), partly acquired. Emphysema develops with no preceding symptoms; in other cases chronic emphysema follows catarrhs, especially the "dry" variety, pulmonitis, aspiration of toxic fumes, etc. In chronic bronchial catarrh with its frequent irritative coughing spells, diminished elasticity is thought of, *i.e.*, weakening of the alveolar walls from increased pressure during expiration while the glottis is closed at the beginning of a coughing spell. In the emphysema developing after pneumonia a partial loss of elasticity is probable, and such injury from pneumonia may develop in childhood as during whooping cough, and only later lead to emphysema. Frequent repetition of acute distensions as occur in asthma seems to cause lesions which finally end in emphysema. Forced expirations, during hard work—lifting of heavy bodies, and especially work when the glottis is closed, as must be the case in glass blowers and players of wind instruments—are considered favorable conditions, or even determining causes. But opinions diverge at this point; many observers do not believe that playing wind instruments has any deleterious influence, (v. Hansemann, lit. v. Baumgarten, Jagic and Lepiner), but Lammel and Erich Becker found increase of the residual air in these players even in the absence of clinical emphysema. Edelmann considers emphysema a condition often combined with a luetic aorta, *i.e.*, it is frequently of luetic origin.

On the other hand, W. A. Freund considers it due to a fixed thoracic dilatation from primary changes in the costal cartilages (yellow shredding, etc.) so that the thorax is fixed more and more in the inspiratory position (see Miura). Since the lungs must follow the thorax, emphysema develops. The author is very skeptical of this opinion, as are Ribbert, Tendeloo, but compare, on the other hand, v. Hansemann. The costal articulations show arthritic changes, partly of a dry ulcerating, and partly of a deforming kind (see von Salis, lit.). According to Loeschke, a more potential role is played by "the round back," *i.e.*, kyphosis of the upper thoracic spine, and the spondylitis deformans of older people which reduces the

length of the thorax, causes descent of the diaphragm and dilatation in the sagittal diameter; (see Passler, Staehelin for a good summary of opinions in reference to emphysema).

(*b*) The so-called vicarious, better, secondary emphysema, appears in those parts of the lungs in which the parenchyma is atrophic, especially in older processes such as fibrous tuberculosis. The healthy parts are more taxed during inspiration and thus overfill and stretch (vicarious respiration). The emphysema once established probably does not produce a true functional balance. The fact that in this secondary emphysema, large bubbles project and are sharply demarkated from the adjacent tissue, adds weight to this theory of origin.

But vicarious emphysema may involve a whole lobe, as the author saw in the left lung of a 29 year old female (atrophied after pneumonia). The lung was riddled with extensive diffuse bronchiectases, fixed to the thorax walls and much smaller than normal, while the right lung was four times as large and emphysematous. Chiari describes enormous "hyperplasia" (numerical increase of alveoli) of a lung, in the presence of complete atrophy of the other. For emphysema in secondary tumors of the lung, see under lung tumors.

(*c*) Senile emphysema, also called atrophic, is secondary to senile nutritional disturbances in the elastic and fibrous tissues; it is caused by rupture of the alveolar walls through no greater pressure than that of normal inspiration.

Emphysematous bullae are visible in this type. Frequently there is marked anthracosis which possibly increases the fragility of the fibrous tissue. But the coal pigment disappears with the disappearance of the atrophic walls so that the emphysematous portions are lighter in color.

The tissues are friable and brittle, the apices and margins are affected, or the lung as a whole becomes atrophic, is dry, flabby, anemic and collapses and wilts on opening the thorax. The thorax itself is diminished in size in contrast to that of true emphysema.

This helps cause the characteristic bent position of the thorax (senile kyphosis), and the sagging of the shoulders in the aged in addition to that caused by the atrophy of the vertebrae. (Comp. the opinion of Loeschke, page 368.)

**Interstitial Traumatic Emphysema.**—The alveoli are torn from gross injury or are ruptured from increased pressure. Air penetrates the interstitial tissue and may spread in the lymph clefts and lymphatics over large areas. Emphysema may develop from sudden marked increase of the inspiratory pressure (air blown in with force, and in all forms of death, with forcible inspiration) as well as with expiratory pressure such as vomiting spells. It is seen especially often in the more fragile lungs of

children, with pertussis and pseudomembranous laryngo-tracheo-bronchitis.

The author also observed the condition in children with acute edema of the glottis, Wassermann and Schwenkerbecher (lit.) in mediastinal pneumothorax and emphysema of the skin in severe influenza pneumonia; Herzog saw it follow an initial coughing spell induced by a foreign body entering the trachea.

Rows or beaded chains of displaceable air bubbles of uneven size usually as large as a pinhead to a linseed are seen in the interlobular septa or below the pleura (interlobular emphysema). Sometimes larger air spaces practically separate the pulmonary lobules (dissecting). The air progressing along the bronchi toward the root of the lung may penetrate the mediastinum, form large bullous spaces in the cellular tissue (mediastinal emphysema) and even reach the skin (subcutaneous emphysema), beginning usually in the jugular fossa and extending over the anterior part of the neck and upper parts of the body, in rare cases also to the abdomen and even to the thighs and knees. If the pleura tears, as in pertussis, a simple pneumothorax results, which, however, is shortly reabsorbed. See under pleura, emphysema of cellular tissue after fracture of ribs.

Extensive subcutaneous emphysema is rare, especially in the thorax and arms, but was seen by the author in a 7 year old girl with acute miliary pulmonary tuberculosis (see also the case of Bevacqua). It has also occurred after intubation (Hammes).

### Circulatory Disturbances of the Lung

**Anemia.**—Anemia is found as one of the symptoms of general anemia. After exsanguination, the lung is pale yellowish white, and if much coal pigment is present in the pleura, the pale surface shows remarkably clear lobular etchings. In emphysema, the pallor of the lungs is due to compression, atrophy of vessels, and disappearance of pigment-containing septa. In the cadaver the anterior parts are usually paler than the posterior parts (comp. hypostasis, p. 373).

**Hyperemia.**—Active congestive hyperemia of various causes is manifested by active filling of the capillaries, as in inflammatory processes such as pulmonitis, and acute disseminating miliary tuberculosis. Heat and cold and various poisonous gases cause congestive hyperemia by direct irritation. The collateral hyperemia, in parts still open to circulation in emphysema, is also of a congestive nature.

Mechanical changes in the pressure relations in the alveoli lead to active hyperemia, *e.g.*, in aeronauts the rarefaction of the air creates a minus pressure in the alveoli and consequently a corresponding plus

pressure in the capillaries inducing hyperemia which occasionally leads to hemorrhage. For the same reason, edema is common.

The intermittent pressure oscillations in the alveoli from regular breathing sustain to a considerable extent the capillary circulation; if these are absent (*e.g.*, in hanging, when inspiration and expiration are stopped) more blood is constantly "sucked" into the capillaries since the alveolar pressure is almost zero, but it is not carried far enough. The heart draws more and more blood from the body and this collects in the lungs with resultant hyperemia and even hemorrhages. From this point of view, the process may be called "aspiration hyperemia." In thoracic paracentesis, if the pleural exudate compressing the lung flows off too quickly, the induced negative pressure within the thorax may cause sufficient hyperemia of the lung to lead to hemorrhages (hemoptysis). For the same reason, the surface vessels of the pleura are torn, because they can not support the sudden excessive inflow of blood. The advent of pulmonary edema is also favored (comp. Ortner).

Passive hyperemia (venous congestion), as a rule, is chronic from cardiac lesions, especially of the mitral valve, but it may develop acutely in cardiac weakness and prolonged agony. The right ventricle undergoes hypertrophy in attempting to establish a balance to regulate the circulation, but the result is incomplete; if insufficiency develops, the congestion progresses to its limit. When the inflow into the left ventricle is impeded as in mitral lesions, or the outflow, as in lesions of the aorta, passive hyperemia distends the pulmonary veins and capillaries. The dilated capillaries are elongated and thus convoluted, and reach into the alveoli (fig. 176), narrowing the alveolar spaces and increasing the consistency of the lungs (red induration).

The convolutions may indeed enlarge the respiratory surface, but since the passive congestion must also involve the bronchi, their lumena are narrowed and less air enters the alveoli.

**Microscopic Appearance.**—The high pressure forces red blood cells through the capillary walls into the alveolar lumena (diapedesis), along with a small amount of serous fluid. Leucocytes and free epithelial cells are also found in the lumena. The latter are detached from the wall by the transudate (desquamation) or are lifted or squeezed off when the alveoli are narrowed; this process of desquamation and new formation constitutes, in fact, a desquamative catarrh (comp. Galdi). The author repeatedly saw isolated, polynuclear, pigmented giant cells (comp. p. 403).

Yellow, brown, or black pigment from destroyed red blood corpuscles lies free within the alveoli or within cells as fine granules, or larger clumps; the cells are chiefly epithelial which swell into large, angular or rounded bodies, often with multiple nuclei, and lymphocytes which wander from

out the vascular system. According to Fr. Muller, they are chiefly descendants of cells from the interstitial connective tissue changed into motile macrophages and invading the alveoli. Pigment granule cells (hemosiderin) may fill some alveoli loosely or thickly; they also appear in the sputum as so-called "herzfehler" cells. But blood pigment is found also in the interstitial tissue (fig. 176), even in the parenchyma, where it lies free in the spaces and in cells of stellate or spindle shaped form; it is usually derived from local capillary hemorrhages but some is brought from the alveoli by way of the lymphatics. Absorbed blood pigment is found even in the bronchial nodes. In rare cases, the capillaries themselves are filled partly with brown pigment masses. These and also those in the sputum give the reaction for iron.

The brown pigment, plus potassium ferrocyanide, plus hydrochloric acid give Prussian blue, the iron oxide salt of hydrocyanic acid (method of Perls). Instantaneous disappearance of the color on addition of alkalies, reappearance by renewed addition of both above reagents, are characteristic.

The pigment, plus ammonium sulphide, gives sulphide of iron (black); method of Quincke. All pigment derived from blood dissolves in concentrated sulphuric acid, to distinguish it from anthracotic pigment. For comparative investigations, see Nishimura. See Ungeheuer and especially Hueck, for iron reactions.

Marchand and Risel described peculiar pigment crystals, light yellow to yellowish red, which turn black during putrefaction; they are probably of analogous nature and are grouped among the iron-containing pigments in the alveoli. They have been seen by the author.

E. Neumann called attention to black (anthracotic) pigment granules covered by hemosiderin of yellowish brown color. He does not believe that hemosiderin undergoes a melanotic metamorphosis. In the alveoli may also be seen concentric laminated or radial striated hyalin bodies, the so-called corpora amylacea. Their origin is under dispute. Friedreich, and later A. and S. Saltykow thought they were confluent erythrocytes undergoing hyalin changes; others think of alterations in epithelial or leucocytic, or lymphocytic cells, see, *e.g.*, Nunokawa, more by Stumpf, Brutt. Corpora amylacea may enclose carbon granules.

When passive congestion is present for some time, the lungs assume a reddish brown color, uniformly or in many spots and foci, projecting somewhat above the section surface. The lung is less elastic, and consequently does not collapse as readily on opening the thorax; it feels tough, indeed almost leathery. The diminished air content of the narrow alveoli reduces the crepitation during palpation. The induration reaches a higher degree in the brown than in the red type and is due partly to the

intense capillary filling and abundance of cells in the narrow alveoli, and partly to the extensive hyperplasia and slighter infiltration of the interstitial tissue (induration of passive congestion) (fig. 176-e). The elastic fibers of all parts progressively increase. The more marked interstitial connective tissue proliferation is in the rust colored foci mentioned, where previous small hemorrhages have been, and where there is much pigment. In consequence, many alveoli are completely atrophic.

Rindfleisch found hypertrophy of the muscular tissue also. In severe cases, the elastic fibers of the large septa and even of the bronchi, vessels and pleura are increased (R. Mills Pearce). Russakoff mentions increase and thickening of the lattice fiber scaffolding.

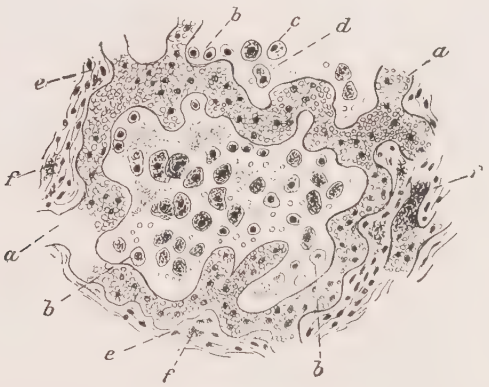



FIG. 176.—Brown induration of lung in mitral stenosis (med. magn.). a, markedly distended and convoluted capillaries in the alveolar wall. Within alveolus fine serum coagulum, red blood corpuscles (d) and larger and smaller cells (bc) with or without brown pigment granules (Herzfehler cells) epithelium and isolated lymphocytes. The interstitial tissue e, cellular infiltrated and thickened. At f, pigment, to the right a vessel, partly filled with pigment.

Hemorrhages occur also from the bronchial veins which are dilated in left cardiac lesions; (comp. on p. 386 infarct of passive congestion).

Relation of pulmonary passive congestion to pulmonary tuberculosis.

Individuals with cardiac insufficiency and pulmonary passive congestion rarely have tuberculosis of the lungs, but, on the other hand, tuberculosis is seen in lungs vicariously supplied by bronchial arterial blood. This old observation was first utilized by Bier in the treatment of tuberculous lesions in the extremities (venous hyperemia due to ligature).

(*c*) Hypostatic hyperemia and hypostasis. When the cadaver is in the dorsal position, gravity causes the blood to sink into the posterior and lower parts of the lungs. But intra vitam, the process is different; in severe illnesses with weak heart, the driving power of the heart and insufficient respiration are not enough to overcome gravity and to keep the

blood in circulation. The blood therefore remains in the capillaries and veins in the lowest levels, not because of gravity, but rather because gravity cannot be sufficiently overcome to carry it onward through the veins.

In the dark, black red, poorly ventilated, air-impoverished parts, absorption atelectasis, transudation of edematous fluid, (hypostatic edema), etc., develop with great ease. Catarrhal changes often follow (hypostatic pneumonia). (Comp. Bartenstein and Tada.)

**Pulmonary Edema.**—This implies saturation of the lungs with serous fluid exuding from the capillaries. The fluid is found mixed with air in the alveoli, from which it may reach the bronchi and the interstitial tissue. It can be made visible by placing at once small fragments of the lung into absolute alcohol or formalin, or by treating it according to Posner's boiling method (placing small fragments into boiling water for 1–2 minutes to coagulate the albumen containing fluid).

Usually, swelling and desquamation of alveolar epithelium are also present, particularly when the edema is of some duration. According to the quality of the fluid, edema is differentiated into:

(*a*) Non-inflammatory, general, usually mechanical, due, as a rule, to stagnation, called passive edema.

(*b*) Inflammatory, accompanying pneumonic processes, sometimes, independently, as an active edema.

The edematous fluid in (*a*) is a transudate from the blood and contains a variable amount of albumen sometimes coagulable; it always contains some scattered red and white blood corpuscles and detached alveolar epithelium.

The edematous fluid in (*b*) is an exudate, richer in albumen, coagulable, and contains more leucocytes and always much desquamated epithelium.

The typical lung of subacute general edema is large, as though in the position of complete inspiration, heavy, firmer than normal and has a gelatinous, glassy gray appearance. From the section surface, a fluid pours out, foamy from intravital admixture with air, but in long standing edema it has less air bubbles, and is clearer and thinner, sometimes red from the addition of blood (by diapedesis) (sanguinous edema). The saturation is often so excessive that palpation suggests a firm infiltration as in pneumonia, but stronger pressure releases a liquid which has been absorbed by the lung, as by a sponge; the finger imprints remain. In fact, the watery fluid runs out in streams from the section surface. The tissue tears easily, is fragile, friable, or soft and jellylike. In the latter case however, the edema is not pure, but shows transitions to catarrhal pneumonia. Bronchi and trachea, mouth and nose cavity also contain foamy fluid.

A transudate may be found in the pleural cavity (hydrothorax) into which dip the posterior and lower parts of the lungs. These parts are often airless and yet edematous.

In quickly developing edema, the blood content is usually increased; in slowly developing edema the tissue is pale. The fluid turns dirty red from post mortem adsorption, dirty gray when there is much coal pigmentation. If the edema appears in the red brown lungs of cardiac disease, the expressed fluid is dirty brown and the condition cannot always be macroscopically differentiated from pneumonia.

In small degrees of edema in the cadaver, the fluid sinks to the posterior and lower parts and perhaps shows no admixture of air bubbles.

### The Formation and the Forms of Edema

General, non-inflammatory edema is an important condition because of its great frequency, and its grave results on respiration.

Acute edema can be differentiated from the chronic form which runs a slower course with repeated exacerbations and which often is one of the symptoms of extensive general serous outpourings.

In a great number of cases, the origin is passive, or cardiac, as in valvular lesions and failure of the left heart, or nephritis; it is a sign of mechanical disturbance of the circulation.

According to Cohnheim and Welch, the edema of passive congestion is due to improper division of work between the right and left ventricles; the left ventricle fails to cooperate perfectly, *e.g.*, in the agonal period, it dies earlier than the right ventricle, or, as in mitral lesions, it becomes insufficient at an earlier time. Cohnheim and Welch in their animal experiments, interfered with the left ventricle by compression with a clamp. The right ventricle continues to force blood into the capillaries, but it flows too slowly from out the left ventricle; consequently transudation takes place through the vessel walls into the tissues; it is literally squeezed through. This theory was illustrated by the rare pulmonary edemas, in which sudden occlusion of the left coronary artery occurred in an otherwise healthy heart; the left ventricle was crippled (comp. the author's observation on p. 57).

In other cases, it is better to assume that an injury to the vessel walls increases their permeability. This is partly true in the general edema of acute and chronic nephritis, although some of it is due to cardiac causes. Some authors assume that vascular changes are present in most cases of passive edema (Sahli, Krehl), but since edema is also observed in intoxications with ether, nitric fumes (Loeschke), war gases, especially phosgene, (Heubner, Groll, lit.), etc., and in sepsis, a "septic-toxic edema" cannot be sharply separated from inflammatory edema (see p. 376).

The occurrence of a neurotic pulmonary edema must also be admitted; it may be experimentally induced by mechanical irritation of the mucosae of the small bronchi and faradisation of lung tissue, or by stimulation of the peripheral stump of the vagus, and thus the vasomotor fibers of the pulmonary vessels.

From all this, it is clear that the general pulmonary edema of many cases can be viewed only as an agonal symptom.

Terminal edema, giving the clinical symptoms of excessive dyspnea, moist rales, and foamy sero-sanguinous expectoration, is seen in cardiac, renal, lung conditions, etc. It impedes respiration, and with failing cardiac activity causes more edema and so contributes to death. Edema at times is acute in its onset and the apoplectic death under these conditions is often called suffocating catarrh, or paralysis of the lungs.

Congestive edema is that which develops readily from acute congestive hyperemia (p. 370). Josselin de Jong saw it kill from asphyxia following the inhalation of steam.

Hypostatic edema follows hypostatic hyperemia (p. 373).

When atelectatic edema occurs in hyperemic tissue, the parts are soft, moist, dark red and spleen-like; non-hyperemic parts appear gray, glassy and gelatinous (see p. 362).

A general pulmonary edema sometimes develops in fat embolism (p. 386) as a (mechanical) passive congestion edema, and may be the actual cause of death.

See Falta and Quittner in reference to the chemistry of various forms of edema.

Inflammatory edema is doubtless due to abnormal permeability of the dilated capillaries; it is mostly a collateral condition in various forms of pulmonary inflammation. Occasionally, it develops independently in severe sepsis.

The fluid is rich in albumen and contains leucocytes, possibly erythrocytes, and fibrin.

The edema in individuals who die some time after a head injury depends on acute inflammation of the respiratory tract due to pyogenic cocci (Kockel), but Jores believes it may be neurotic in origin.

During the first stage of a typical fibrinous pneumonia, the inflammatory edema and congestive hyperemia dominate the picture. If the edema continues during its course, the disease is spoken of as serous pneumonia. Edema may exhibit another very dangerous relationship to pneumonia (lobar), and that is when it appears acutely in the non-consolidated areas. The result is usually fatal.

In poisoning by war gases there is direct pulmonary injury followed by very severe inflammatory edema, which is the cause of death. The lung

is distended and the right heart dilated. Numerous small bronchopneumonic foci may be present. Death usually occurs in twelve to twenty-four hours (see B. Fischer and Goldschmidt). According to Ricker, Heubner and others, extreme cases develop stasis throughout the lungs accompanied by acute cardiac failure; in less severe types, there is a prestasis (Ricker), *i.e.*, slowing of the blood circulation, which, if the duration is longer, induces marked exudation, *i.e.*, pulmonary edema. (Details in reference to war gases by W. Koch and Groll.)

**Translator's Remarks.**—An important question is the ultimate result of war gas poisoning. The evidence is in favor of the opinion that little or no permanent injury results on recovery. According to Koontz, experimenting with dogs, permanent damage consists of focal areas of lung fibrosis, thickening of bronchial walls and occasional obstruction of bronchioles but in amounts scarcely sufficient to affect the function of the lungs (Arch. Int. Med., 36: 204: 1925). Gassing probably has little or no effect on subsequent pulmonary tuberculosis; see Mil. Surgeon, 50: 609: 1922. Francine, A. P., New York M. J., 117: 25: 1923 and Francine, A. P., testimony before Senate Committee, Mil. Surg., 54: 470: 1924.

Incurable Edema. Chronic edema is non-absorbable because of atrophy of lymph vessels, or interstitial changes as in anthracosis or tuberculosis; the fluid is thick and gelatinous in consistency. Yellowish white specks can be recognized macroscopically in the gray glassy masses.

Microscopically, the epithelial cells and leucocytes are undergoing fatty degeneration, or the leucocytes are loaded with fat granules (fat granule cells). To be exact, this is not always fat, but doubly refracting fatty substances which appear during cell disintegration (see ref. to this under kidney). The picture may develop as well from simple edema as from occlusion atelectasis or from inflammatory edema, although the latter, as a rule, shows more cells in the alveolar contents, chiefly leucocytes undergoing fatty degeneration.

Occasionally, a similar event occurs during the course of catarrhal pneumonia, but it is interpreted differently, and is called chronic catarrhal pneumonia (Virchow). Compare p. 408.

**Hemorrhages into and within the Lung Parenchyma.**—When blood from the nose, mouth, etc., reaches the lungs by aspiration, diffuse, lobular, approximately wedge-shaped, bloody foci are found in the lower lobes. When small, they are absorbed without any consequences, but pneumonias may develop from them.

Traumata, being run over, concussion, fractures of ribs, bullet wounds may produce rhexis hemorrhages with more or less marked destruction of lung tissue. The same occurs in pressures during explosions (comp. Rusca, lit.). Contusions of the thorax may produce no immediate symptoms, but post traumatic bronchogenous pneumonias may develop (comp. Sternberg); the same occurs in indirect lung injuries from projectiles (comp. Merkel). Compression of the trunk (in a surgical sense) produces characteristic obstruction hemorrhages of mucous surfaces, skin, and deeper tissues of the head, throat, and neck, more rarely the brain (Leupold, Bantelmann), distant from the point where trauma was inflicted, but, as a rule, the lungs escape (pressure congestion, Perthes; comp. Marchand, lit. Leupold).

In the course of disintegration of the parenchyma, such as in gangrene, syphilis, carcinoma, and especially caseous tuberculous softening (comp. tuberculosis), hemorrhages occur; if pure blood is coughed up it is called hemoptoe, if mixed with sputum, hemoptysis. Hemorrhages of the first type also come from bronchiectases, echinococcus, rupture of large aneurysms, rarely from ruptured anthracotic bronchial nodes, or rupture of the pulmonary artery (Harbitz).

In some inflammations, such as the severe septic bronchopneumonias of scarlet fever, diphtheria, anthrax, etc., the exudate may be hemorrhagic.

Hemorrhages also come from capillaries and peribronchial veins in circulatory disturbances such as suffocation, when they are usually not large, but multiple, or hemorrhagic infarction and fat embolism, in some poisonings, in the hemorrhagic diatheses, or even as supplementary or vicarious to the menstrual flow (menstruation metastasis). The latter are considered due to vascular dilatations of nervous origin via vasomotor influences and are called neurotic, or neuropathic, or angioerethic, from stimulation of the dilatators.

Although the exact relations are still obscure, it has been proved beyond doubt in animals as well as humans, that certain disturbances of the nervous system are causes of neurotic hemorrhages in several viscera, especially the lungs and stomach, but also in the esophagus and liver (see v. Recklinghausen's text book, and Marchand). In diseases of the pons, the medulla oblongata, other parts of the brain, in both spontaneous and traumatic hemorrhages, the cranial nerves (vagus, trigeminus), the cervical sympathetic and cerebral bullet wounds, numerous hemorrhagic foci to the size of cherries may appear in the lungs; they have been observed repeatedly by the author. According to Ricker and Hesse (lit.), these pulmonary hemorrhages may be explained by correlated processes in the nervous system of the pulmonary vessels. (Comp. lit. under stomach.)

**Hemorrhagic Infarction.** *Embolic, and the Rarer, Thrombotic Infarction.*—Hemorrhagic infarction is due to obstruction of a branch of the pulmonary artery. The areas (Laennec) are firm, slightly prominent under the pleura, seldom bossed, in dark outline, chiefly in lungs showing red or brown induration, *i.e.*, the lungs of cardiac disease, usually of moderate size (cherry to a walnut) and occasionally involve more than half of a lobe. Rarely single, they appear by tens or twenties. The sharp margins of the lung, especially the borders of the interlobar clefts, are selected. Infarcts are most frequent in the lower lobes, but also occur in the middle lobe of the right lung.

The predilection of the lower lobe depends on the width of its pulmonary artery. It has not been verified that the lower lobes are favored chiefly by emboli from the inferior vena cava, and the posterior upper portions by emboli from the superior cava (injection experiments of Kretz, Helly). (See, among others, Borst, Hofmann, Reye, Ribbert, Alwens and Frick, lit., Schonberg, Rupp; comp., in opposition, Burger and Strassmann.)

On section, the foci are wedge-shaped, the apex pointing to the hilum where the vessels enter, and the base directed to the pleura. Over the infarct, the pleura is soon covered with a delicate layer of fibrin (pleuritis); the color is black red to sepia, the section surface is smooth, the focus is airless. Only in the early stage can dark, thick bloody fluid be expressed; later it becomes dry, peculiarly smooth, homogeneous, devoid of any alveolar structure, and harder in consistency due to coagulation necrosis. On section, the apex of the cone reveals a bronchus, and in most cases a branch of the pulmonary artery occluded by an embolus with perhaps secondary thrombosis, or rarely by autochthonous thrombosis. A vein is often closed by thrombosis.

Infarcts are clinically indicated by blood red sputum, later by many pigment cells (see p. 372).

Microscopically, fresh infarcts show the alveoli filled with clotted blood, closely packed red cells, isolated leucocytes and fibrin threads. In unstained slides especially, hyalin thrombi are seen in many capillary branches; Weigert's stain discloses that they consist mostly of thready fibrin masses fused with the walls. Other capillaries are filled with blood, and still others are empty. When the infarct is somewhat older, nuclear staining plainly shows that the lung tissue is necrotic within the infarcted area. Sometimes leucocytes gather at the periphery.

**Formation.**—There is great uncertainty in reference to the causative processes. It is generally assumed that stasis in the veins and capillaries of the lung causes the typical hemorrhagic infarcts, *i.e.*, especially in consequence of left cardiac lesions. If a branch of the pulmonary artery

is suddenly occluded in a lung with passive congestion, the result is that not only are the vessels of the conical area supplied by the branch filled with blood, but all of the tissues are saturated. From where does this blood come?

Cohnheim assumed that the pulmonary venous blood flowed backward (venous reflux) and first filled all the vessels, then passed through the vessel walls which had been altered by the preceding ischemia. But investigations by v. Zielongo, Litten, etc., have not verified this idea, since it was found that infarction also took place if the artery was ligated with the vein. The opinion of Grawitz, that the blood came from newly opened peribronchial, subpleural and intralobular capillaries from the bronchial arteries, has also not been demonstrated (comp. Orth, and see Geigel).

As represented by Marchand, the first process is stasis in the arteries and veins of the occluded area, stasis because of the difficulty in outflow due to congestion of the cardiac base. But stasis occurs not only in the pulmonary veins, but also in the overfilled bronchial veins and this is, of course, transmitted to the pulmonary veins since the bronchial veins empty into the latter (see p. 339). Propulsive power is lacking to force the blood past the resistances. As is well known, the pulmonary arteries are end arteries with but few larger anastomoses among them.

In a non-congested lung, embolic obstruction of the pulmonary artery does not cause permanent disturbances, since, at first, the area is ischemic and is quickly supplied with blood through the anastomoses between the bronchial and the pulmonary arteries, and through capillaries of adjacent free branches of the pulmonary artery. The essential difference between the first result of embolic occlusion in a normal lung and in one with passive congestion is this: in the former, the blood is able to flow into the veins if the total energy, *i.e.*, cardiac power and suction in the veins, is sufficient to overcome the resistance in the capillaries; the area, although ischemic at first, as stated above, is quickly resupplied with blood. It is only exceptionally that this reestablishment of circulation does not occur, and then an anemic infarct is developed. Tendeloo mentions their occurrence in older persons who have no passive congestion, and the author has seen such cases. Insufficient arterial pressure, poor condition of arteries, etc., serve as explanations (see Thomas, lit.). But in pulmonary passive congestion, ischemia is not present at any time, the excessive venous pressure prevents outflow and causes stasis of the blood current. When this is present, the collateral inflow from bronchial arteries and adjacent capillaries cannot enter the infarcted area, because the blood pressure cannot be increased sufficiently to reestablish normal circulation. There is also the possibility of reflux of blood from the bronchial veins which is under

higher pressure, as emphasized by Koster (but denied by Geigel), than the blood in the area of stasis. This inflow of blood from every side causes extreme congestion, hyperemia, excessive filling of capillaries, then stasis, and finally diapedesis of blood corpuscles so that the air spaces are filled with blood and left airless. This constitutes the perfect hemorrhagic infarct. Since circulation stops completely, the infarcted area dies (necrosis). As long as the blood in the alveoli is not coagulated, some may enter the bronchi (bloody sputum).

Probably, multiple local stases and thrombi are also present to add to the circulatory congestion. v. Recklinghausen, in particular, emphasized the importance of these smaller impediments, especially hyalin thrombi. They help to explain cases in which typical infarcts follow septic emboli, or cases in which substances appear which cause coagulation, although no general circulatory disturbances (congestion) are present in the lungs. It is supposed that the thrombi form in arterial branches, capillaries and minute veins, making impossible a quick collateral equilibrium; the small collateral currents which strive to reach the area meet obstruction everywhere until stasis and diapedesis set in. But it must also be borne in mind that septic hemorrhages may be caused by toxic injuries of the capillary walls. At any rate, even without embolic occlusion, hemorrhagic infarction is possible, although these infarcts are never so sharply circumscribed and macroscopically visible as the conical ones, encountered on closure of an arterial branch.

**Translator's Remarks.**—For the relation of the pulmonary and bronchial circulation see Ghoreyeb, A. A. and Karsner, H. T., J. Exp. Med., 18: 500: 1913. For infarction, see Karsner, H. T. and Ash, J. E., J. Med. Res., N. S., vol 22, 205, 1912 and Karsner, H. T. and Ghoreyeb, A. A., J. Exp. Med., 18: 507: 1913.

### Consequences of Occlusion of the Pulmonary Artery. When is Occlusion by Non-infected Emboli Followed by Infarction?

Embolic occlusion of the pulmonary artery is not always followed by infarction, especially if the smaller branches are plugged, because collateral capillary anastomoses are opened at once, not only between the pulmonary and bronchial arteries, but also between the capillaries of the peripheral bronchial artery and those of the pleura.

Occlusion of branches of the second and third orders is usually followed by infarction because there are only capillary collaterals in the lung, and arterial anastomoses are lacking. But even then, the consequences of embolism may be absent if the lung is healthy and the cardiac reserve is sufficient. (Comp. animal experiments by Fujinami, Orth, Zahn.) The

collaterals are able to substitute quickly enough to prevent a longer interruption of the circulation; on the other hand, when passive congestion is present, hemorrhagic infarction occurs.

Occlusion of even a main branch of the pulmonary artery is not necessarily followed by infarction, because dilatation and response of the bronchial artery may occur in front of the obstruction (this artery also supplies the parietal pleura), help being obtained from the tracheo-esophageal, pericardial, phrenic and mediastinal arteries.

But when the main trunk of the pulmonary artery, or both main branches are occluded, almost instant death results. Among other conditions, this is seen in varicose veins of the legs, especially during pregnancy, or during an otherwise satisfactory puerperium, or post operatively (lit. by Thorel), after clean surgical (see Ranzi, lit.), particularly gynecological, operations (comp. Gessner, Fehling—chief cause cardiac weakness), especially for myomata or even curretage. It frequently occurs during the first attempt to rise from bed—to use the commode, bathe, etc.,—or even after mere resting in bed for several days; it has been observed in other patients afflicted with various internal diseases. It is usually due to emboli liberated from thrombi on the valves of the femoral veins. A fatty heart is often found. Later in life, the frequency of thrombosis and embolism increases considerably. As a rule, it is not logical to assume there are inflammatory factors in this thrombosis (see Kretz; Aschoff), but infection and injury surely play a part (see Hampton and Wharton). Prophylaxis consists of elevation of the legs (Lennander), movements of the legs and early rising (Kummell), breathing exercises, etc. (lit. by Zurhelle, Hoffmann), avoidance of every pressure, every compression or constriction of the legs by the usual suspension of the knees in gynecological treatment (Zweifel); attempts to lower the coagulability of the blood are recommended (Ribbert). For the operative removal of the embolus, see Trendelenburg, Ulrichs.

To make sure that embolism of the trunk or the two main branches of the pulmonary artery is not overlooked at autopsy, it is advisable to incise the pulmonary artery in situ from the right ventricle onward before the heart is removed. Blood cannot enter the left auricle since it is paralyzed (comp. Kose), while the right ventricle is filled to its maximum capacity. According to Strueff, the most important factor is suspension of the lesser circulation which causes a sudden fall of pressure in the greater circulation. Others think death is due to asphyxia (lung death), (see experiments by Schumacher-Jehn). In marasmic individuals with weak cardiac action, or in those with pneumonia or ulcerative tuberculosis in the other lung, sudden occlusion of the trunk of one pulmonary artery or of a larger branch is often fatal; stronger individuals may escape.

When the main trunk is occluded gradually, the bronchial artery may substitute sufficiently well to allow continuation of life (Kuttner, Hart). This is analogous to the conditions in congenital pulmonary stenosis (see p. 91).

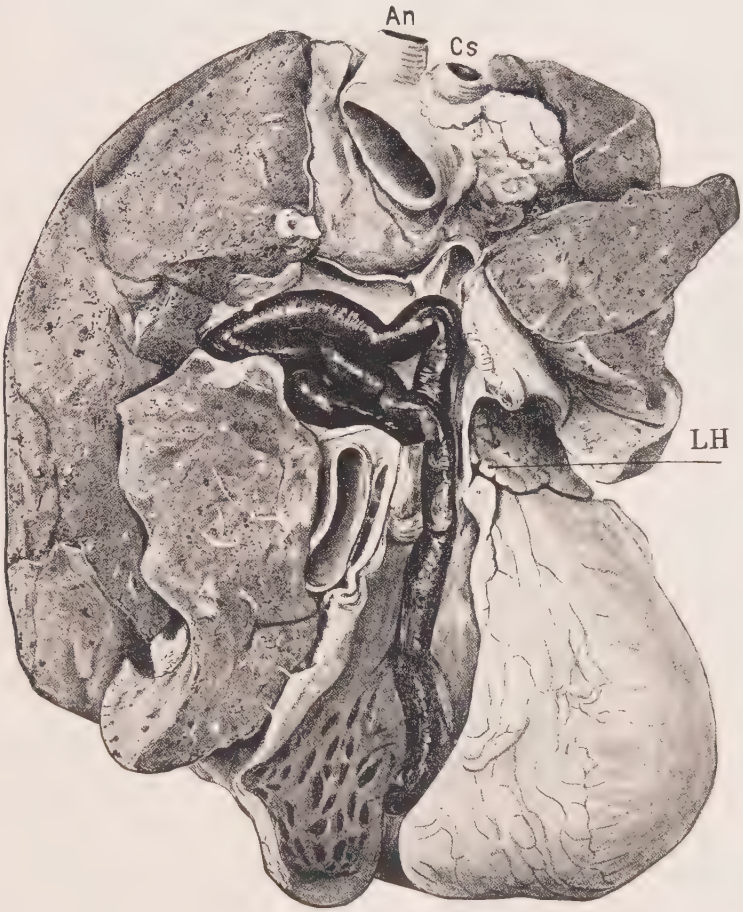



Fig. 177.—Embolism of pulmonary artery from thrombosis of femoral vein. Opened right ventricle from which the long worm-shaped blood plug enters the pulmonary artery (one leaflet visible) and continues in convolutions in its main branches. The convolution occluding the l. pulmonary artery contracted later and the arterial inlet is open. LH, left auricle; on same level on the right side long oval cross section of aorta which fits on the aortic cross section seen above in the picture; An, innominate art.; Cs, left common carotid. The end of the long embolus which passes through the tricuspid valve into the right auricle is not visible. Woman of 62 years. Quick death, 16 days after a gynecological operation (colporrhaphy on account of prolapse); about ½ nat. size.

## Source, Forms and Regression of Emboli

Emboli are derived from thrombi of the right heart or the veins of the body, especially of the legs and even more frequently, the pelvis, *i.e.*, the female and male genitalia (uterine—spermatic—prostatic veins).

A long thrombus, not as large as the diameter of the pulmonary artery, usually red, *e.g.*, from the saphenous vein, may enter the pulmonary artery in such a way that it becomes looped and is forced into several branches. A long narrow plug may be coiled and thus occlude a large main trunk. Sometimes the central end of the embolus shows a fracture surface which fits exactly to another belonging to a thrombus still lodged in a vein, and thus the origin of the embolus is absolutely demonstrable. The central end may be recognized as its head by its light color and laminated structure (precipitation thrombus) differing from the rest, the tail, which is dark red and essentially a coagulation thrombus.

An embolus frequently is lodged across an arterial bifurcation (riding embolus) causing only unilateral occlusion or none at all, but a secondary thrombus may be superimposed. The embolus is transformed in loco, *i.e.*, is organized from the base and remains permanently as a strand, thread, string or plate (sometimes saddle-shaped) passing through brown, yellow and white colors.

Occasionally it is difficult to distinguish between an embolus in the pulmonary artery and a post mortem clot, particularly if the embolus is a quite fresh red thrombus (coagulation) detached from the femoral or iliac vein (see Marchand). But a red thrombus usually shows the structure, however slight (microscopical), of the grayish white deposition thrombus (platelet columns and leucocytes in delicate arrangement). It fills the lumen more firmly than a coagulum. The difficulty is increased by the deposition of post mortem clots on the embolus. White clots can hardly be mistaken for emboli (thrombi fragments), but according to Tendeloo, lardaceous coaguli forming sub finem may enter the pulmonary artery and cause sudden death.

### Later Conditions in Hemorrhagic Infarcts

Normal Course. (*a*) Complete Absorption or (*b*) Healing with Organization and Cicatrization.

(*a*) When the infarcted area is small and the adjacent lung tissue not atrophic, the extravasated blood may disappear completely in some weeks, at most, leaving a slight pigmentation and thickening. But if the infarct dies, the area is discolored, brown and rusty, with a yellow edge at its margins, due to fat infiltration, and a reactive inflammatory wall around the periphery. Vessels and granulation tissue then grow from the periphery into the infarct. The necrotic, disintegrated masses are absorbed (in weeks), granule cells appear, and their place is later occupied by granulation tissue. This process is called organization of the infarct. Cicatricial change begins after this, starting at the periphery as a gray edge and gradually extending into and throughout the whole area.

Finally, the place of the infarct is taken by a wedge-shaped, ultimately almost linear, deeply contracted scar, which probably gives no hint as to its origin. But sometimes it contains necrotic rests or isolated alveoli and bronchi. The artery obliterates, but is occasionally recanalized (see p. 120). The pleural layers are adherent, or the visceral pleura is thickened.

**Irregular Course of Hemorrhagic Infarcts.**—A general pleuritis may be spread from the base of the infarct and serofibrinous, hemorrhagic or purulent exudation compresses the lung.

In decrepit individuals, the infarct may disintegrate and soften into non-putrid debris, without organization. This is rare, but dangerous on account of subsequent pleuritis or perforation of the pleura. The possibility of the formation of a true anemic infarct must not be ignored (see p. 380 and comp. Westphal).

If secondary pus formation or gangrene should occur in the periphery, the infarct may be completely isolated from the healthy adjacent tissue and appear as though shelled out (sequestration), see fig. 178.

FIG. 178.—Hemorrhagic pulmonary infarct with sequestration, demarkating abscess and pleuritis (empyema). 35 year old woman with cardiac lesions (stenosis and mitral insufficiency); $\frac{4}{5}$ nat. size.

Pulmonary infarcts, by their communication with the bronchi, occupy a position different from other infarcts; pyogenic or putrefactive organisms spread through the bronchi, and produce abscesses, and gangrene. Suppurative pleuritis and empyema may develop from very small peripheral foci.

Calcification is rare and occurs chiefly along the borders in vessel walls, capillaries, interstitial tissue and bronchial walls. Exceptionally, the entire infarct becomes a firm, dense concretion. In the rare cases of lime incrustation in "calcium metastasis" (Virchow; destructive processes in the skeleton), or even in "heterotopic calcium incrustation" (Kockel, lit.; without skeletal destruction or previous local pulmonary change), the lime seems to have a peculiar affinity for the elastic fibers which are diffusely infiltrated, or granular, and perhaps fragmented. (In reference to this calcification of infarcts, elastic fibers, even alveolar epithelium, see Huech, and in general, see Kischensky, Huebschmann, Tschistowitsch and Kolessnikoff, Pari, Bittrolff, M. B. Schmidt.) In an old woman with very advanced osteoporosis, the author saw a gritty calcified infarct the size of a child's fist. In a 31 year old woman with uterine carcinoma, an embolic lung focus of the character of pumice stone showed calcification in septa, vessels and emboli. In a rare case of Verse (chronic myelogenous leukemia), the pulmonary veins and the left auricle were both calcified

to a most marked degree (see also Verse, calcinosis universalis, and Harbitz, lit.).

(*b*) **Infarction Due to Blood Stasis.**—Bloody saturation and hemorrhagic infarction can be due to obstruction to the outflow of venous blood. Smaller capillary hemorrhages have been mentioned as frequent findings in cyanotic lungs, but larger diapedetic hemorrhages also occur which produce infarction in the tissues; the area is more diffuse in its boundaries than an arterial infarction.

The caudal anterior sections are sometimes preferred; since they are prone to hypostasis in the decrepit who may be in the dorsal position. From hypostasis there may also develop congestive infarcts beyond the region of stasis and diapedesis.

Termination. Smaller hemorrhages disappear by absorption; larger ones leave pigmentations and thickenings of lung tissue, but the structures remain recognizable. Occasionally, an artery is occluded by a thrombosis extending retrograde from the infarct.

### OTHER EMBOLIC PROCESSES IN THE LUNGS

**Infectious Embolism.**—When emboli contain pyogenic or putrefactive organisms, and even completely occlude an artery, the inflammatory changes so overshadow the mechanical sequences from the very beginning, that the latter are often indistinct or non-existent, (comp. p. 379). Arteritis and periarteritis are usually the first changes and are followed soon after by purulent or necrotic inflammation of the actual lung tissue.

These are spoken of as embolic purulent or gangrenous foci, or as embolic or metastatic suppurative and gangrenous focal pneumonias.

In some cases, however, the first process is necrosis followed promptly by suppuration which separates the necrotic wedge and shells it out (as in fig. 178) to be expelled; or it suppurates in situ.

Sometimes capillary bacterial embolism is found in pyemia with no macroscopic changes in the lungs.

**Fat Embolism** (Comp. p. 207).—During the destruction of fatty tissue, fluid fat may enter capillaries or veins rather than lymph channels (E. O. Schultze), which of course empty into veins via the thoracic duct (Fritzsche). After passing through the right ventricle most of the fat is lodged in the lungs. The shower may occur for days; the capillaries are markedly distended and the small arteries plugged with non-infectious, sausage-shaped bodies. As a matter of fact, fat globules are frequent emboli, usually in small quantities, and without results. The most frequent sources are (1) from the bone marrow in fractures especially of atrophic bones with abundant fat, but also from surgical manipulations, forcible pressure, readjustment of ankyloses, especially of the knee, and even from purely

local or general concussions of the body, *i.e.*, of the skeleton, without fracture (Ribbert, disputed by Bergemann), or from suppurative osteomyelitis, (2) from contused subcutaneous fat (in delirious patients), or any kind of injury, and in eclampsia, (Virchow, Schmorl), (3) from the pelvic fatty tissue, as during childbirth, from fatty abdominal tissues following laparotomies (Praeger), (4) the fat of the liver may be carried away after crushing trauma to the organ, (5) moderate pulmonary fat embolism follows extensive destruction of the brain, (6) from fatty softening of thrombi, etc. According to Carrara, it occurs in many cardiac, renal and vascular diseases, and also in burns (46%) and scalds of soft tissues (see under skin), as experimentally verified by Foa (see lit. by Frischmuth, Gaugele-Risel).

FIG. 179.—Fat embolism in capillaries and intra-alveolar vessels of the lung due to fracture (crushing) of several bones; fresh preparation; (medium magn.).

Some of the fat may pass through the lungs, especially if the quantity is large (respiratory disturbances), and may then enter other organs such as the kidneys, brain, heart, spleen, pancreas, etc., or rarely, even into the retina and skin, (with flea-bite hemorrhages) (comp. Benestad, Fromberg). It takes large quantities of fat in the lungs to cause death, and then not suddenly as in animals (comp. Fuchsig), but after some days, or subsequent to repeated large additions, possibly caused by manipulation of the patient, especially one with multiple fractures, until about one third of the lung is blocked. In such cases, pulmonary edema and petechial hemorrhages appear, and more rarely, larger hemorrhagic infiltrations. Petechiae of the pleura are frequent. The lungs are not changed macroscopically by fat embolism, and therefore it must always be hunted microscopically. In pronounced cases, however, fat droplets are found in the pulmonary arterial blood.

Embolic fat disappears slowly, part is absorbed in loco subsequent to saponification, part is carried by wandering cells from the pulmonary capillaries to the lymphatics (Beneke, Wuttig, Possati). A considerable part, according to Burger, the main body, reaches the general circulation

through the pulmonary capillaries and is then absorbed and partly excreted by the liver, and by the renal glomeruli into the urine (lipuria).

Occlusion of numerous coronary vessels and especially cerebral vessels (anemic necroses, petechial hemorrhages) may itself, or combined with fat embolism of the lungs, cause death. According to Grohndahl, in fatal cases of fat embolism, 54% are pulmonary (respiratory), and 46% cerebral (see Maida).

Fat cells are rarely carried off.

**Pigment Embolism** (see p. 206).—Pigment emboli from ruptured, pigmented, softened bronchial lymph nodes occasionally enter a branch of the pulmonary artery; it is relatively common to find thinning and bulging of the pulmonary artery through which hard or soft lymph nodes shine as bluish black masses; the arterial wall (pulmonary) may even be spotted with pigment deposits. It is often seen in the trachea and bronchi. If the lymph nodes or pigment masses rupture into veins within the lung, pigment transport results, especially to the spleen (see p. 222) and liver, but also to the bone marrow and kidneys (Weigert).

**Air Embolism and Gas Embolism** (see p. 207).

**Tumor Embolism** (see under tumors of lungs).

**Other Cell Embolisms.**

Capillary emboli of liver cells from ruptured livers are rare (lit. by Hess), but embolism of placental cells is relatively frequent during pregnancy and post partum (see experiments of Maximow, etc., under placenta). The transport of megacaryocytes from the bone marrow (p. 286) is extremely frequent (parenchymatous embolism, Lubarsch); they appear as bizarre, chromatin-rich nuclei in the capillaries of the lung (Aschoff, lit., and experiments by Sapegno, Ogata). Cell embolism can be seen after trauma and during the course of various, especially acute infectious, diseases, and, as frequently seen by the author, in most bronchopneumonias of whatever etiology, and in other conditions such as passive congestion. Some reach the greater circulation and enter the liver, spleen (comp. Hedinger), and especially the renal glomeruli (see Casaris-Demel). They perish after some days.

### Inflammation of the Lung

**Fibrinous Pneumonia, So-called Lobar Pneumonia.**—Fibrinous, also called croupous, lobar, or true pneumonia, is an acute inflammatory infectious disease with sudden onset appearing in epidemics or sporadically. It is characterized anatomically by an exudative inflammation with coagulation into a cohesive mass of hemorrhagic fibrinous exudate within the alveoli, infundibuli, and usually also in the smaller bronchioles. This stiff exudate fills the spaces with plugs, and as long as they remain

solid, the section surface has a granular appearance because the contents of the alveoli and infundibuli are forced forward as granules from slight retraction of the elastic alveolar walls (granular pneumonia).

These granules appear more plastic if the tissue is torn. The diameter of the infundibular plugs approximates one millimeter.

The process involves at least a whole lobe or its largest part (lobar pneumonia), and the changes are frequently symmetrical, as if molded, but it must be emphasized that there is only a quantitative extension of this process (Ribbert) in comparison to the lobular type, *i.e.*, bronchopneumonia. The latter has a peculiar feathered appearance, but there are cases in which the pneumococcus produces smaller lobular foci of inflammation, and others in which the section surface of a completely hepatized lobe still shows the confluence of complexes of smaller foci. The tendency to rapid, massive, localized, lobar infiltration, however, is characteristic only of true pneumonia. Of course, the term "lobar" must not be taken too literally; not rarely the pneumonic process does not respect the interlobular fissures, but passes over them and stops in the neighboring lobe, usually horizontally circumscribed. According to the plausible opinion of those who suppose lobar pneumonia is a bronchogenous infection (Tendeloo, W. Muller and others), the inflammatory process extends at once from the bronchi by way of the septa and lymph spaces to the alveoli. Carnot attempts to explain the lobar localization which is not easily explicable, by assuming that a reflex started by a small pulmonary focus extends to the bulbo-medullary centers and then to areas corresponding to determined segments of the lung, where the pneumonic inflammation, which shows a segmentary topography, is then established.

**Causative Factors of True Pneumonia.**—The etiology is not quite uniform, but usually there is found A. Frankel-Weichselbaum's diplococcus pneumoniae,—lanceolatus, also called pneumococcus, or streptococcus lanceolatus capsulatus pneumoniae (fig. 183). In rare cases, prognostically unfavorable (Toenissen), Friedlander's bacillus pneumoniae or bacillus mucosus capsulatus is found, the organism which at first was considered the chief cause of pneumonia (comp. Kokawa and Stuhlern), or the streptococcus pyogenes, or the variety related to lanceolatus, and designated streptococcus mucosus. K. Koch calls this organism "pneumococcus mucosus" because it belongs to the pneumococci; it was observed several times by the author, as the cause of croupous pneumonia (lit. by Otten, W. H. Schultze, Haas, M. Frank). Less often the staphylococcus pyogenes aureus is discovered, but then the inflammation spreads more in foci, usually with abscess formation and purulent pleuritis, especially during childhood (comp. Schottmuller). Sometimes several microorganisms appear together such as influenza bacilli and pneumococci, very

rarely influenza bacilli alone. For sarcinae tetrageni as a rare cause of pneumonia, see Pollak, lit.

### The Diplococcus Pneumoniae or Pneumococcus and Its Properties

It is a rounded, later oval, or lancet shaped organism usually occurring in pairs, or like streptococci in chains of three, four or more links. It is non-motile. In the animal body and in sputum it has a mucous capsule, not found, as a rule, in artificial cultures. Propagation by culture has some difficulties since it grows only at a temperature above 24° C. and growth ceases at 42° C. Friedlander's bacillus of pneumonia, on the other hand, grows at room temperature. Cultures (glycerin agar is best) often die, and their virulence can be fully preserved only by frequent passage through suitable animals. Their characteristic form which is completely lost by repeated transplantation on culture media may then be regained (Kruse and Pansini).

It is pathogenic for mice, rabbits, etc., which die of septicemia (comp. Kindborg).

The pneumococcus of A. Frankel-Weichselbaum is Gram positive, while the pneumo-bacillus of Friedlander is Gram negative. Pneumococci are found in the sputum of pneumonia patients both free and intracellular; they are especially numerous during the stage of red hepatization and disappear later.

### How Does the Diplococcus Pneumoniae Reach the Lungs?

Pneumococci are often the cause of focal pneumonias, and of lobular extensions (see p. 404), furthermore, of serofibrinous as well as purulent, fibrinous and perhaps, especially if weakened in its virulence by the resistance of the organism, pure suppurative exudation, especially in serous membranes, *e.g.*, peritoneum. In the kidneys, they may give rise to acute nephritis. They produce various kinds of inflammation of the cornea, among them, the serpiginous corneal ulcer; they also produce osteomyelitis (see there).

The pneumococcus is also able to cause serofibrinous or purulent meningitis independent of pneumonia. Probably some cases of so-called epidemic cerebrospinal meningitis are of this etiology, instead of the more usual one.

A diplococcus pathogenic for mice (cocci of sputum septicemia) perfectly analogous to the pneumococcus is often found in the nasal secretions and mouth cavities of healthy people; it is very frequent in diseases of the nose and the sinuses, or the tympanic cavity, in children particularly. Thus the appearance of sporadic cases of pneumonia is easily understood. If a predisposing factor appears, *e.g.*, a cold, (see Tendeloo, Schade), or

trauma which possibly causes minute or more substantial tissue lesions (blow, pressure, see Lichtschlag), or circulatory disturbances, it enables the pneumococcus to penetrate the lungs, or possibly, if already present but latent, to become activated and develop its pathogenic activity. Compare contusion pneumonia in hemorrhages, p. 378. The portal of entry cannot always be demonstrated; it is believed to be aspiration. But it is certain that true aspiration pneumonias such as develop after ether anesthesia, apoplexy, uremia, etc., are different from typical pneumonia. There is absence of herpes, the initial chill and the characteristic fever, and in these cases pneumococci are not present in the lungs or are soon destroyed. For these reasons, direct entrance of pneumococci into the blood with subsequent growth in the lungs appears a more logical assumption. Rigor is, of course, a certain hematogenous symptom as the pneumococcus enters the circulation. Pneumococci are frequently found in the herpes labialis; and since the pneumococci in the mouth cavity in typical pneumonia, are exceedingly virulent, invasion of the blood stream probably occurs from here (see Klipstein and especially v. Calcar).

### Complications ("Metastases") of Pneumonia

**Pneumonia as a Complication ("Metastasis") of Other Infectious Diseases.**—The complications in other organs may be pleuritis, which is a regular accompaniment of pneumonia, peri- and endocarditis (see pp. 15 and 35), peritonitis, meningitis, nephritis, inflammations of the bones and joints, etc. Pneumococci are found everywhere; indeed in pneumococcemia or pneumococci sepsis, endocarditis or menigitis is a common finding. But the organisms may enter the blood stream in croupous pneumonia without such grave septic consequences. Other pyogenic bacteria are occasionally found as a mixed infection usually bronchogenous. In many cases no complications are present except pleuritis.

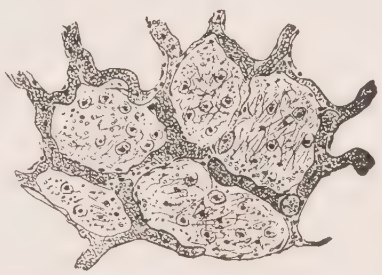


Fig. 180.—Explanation in text.

In still other cases, an existing infectious disease is complicated by pneumonia. These pneumonias may appear in articular rheumatism, osteomyelitis, influenza, meningitis, typhoid fever, etc., and the same bacteria are found in all affected places. But various types of bacteria may be found in the lung at the same time, probably as an expression of a bronchogenic mixed infection. Thus in pneumonia with typhoid fever, besides typhoid bacilli, the pneumococcus or common pyogenic cocci are also found in the lungs.

The course of fibrinous pneumonia is usually quite typical; three stages are recognized: (*a*) congestion, (*b*) hepatization, (*c*) resolution.

(*a*) In congestion, engorgement (Laennec), or the hyperemic-edematous stage, the alveoli contain a serous exudate (inflammatory edema) with many erythrocytes, some polymorphonuclear leucocytes, exfoliated, large, swollen epithelial cells and necrotic hyalin plates of alveolar epithelium. Fibrin threads soon appear, and as the disease develops, become more and more numerous, while epithelial participation diminishes. The capillaries are filled to the limit.

See Pratt in reference to special cell forms, especially large phagocytes, probably epithelial, often showing two to four nuclei, and containing leucocytes and lymphocytes, rarely erythrocytes, also diplococci, which appear during this stage and likewise in gray hepatization.

The lung is filled with blood, is dark bluish red, somewhat heavier than usual. From the section surface, a turbid, somewhat thick viscid grayish red, slightly foaming fluid can be expressed while the air content is decreased. The tissue barely crackles under pressure, but small sections may still float on water.

The sputum is like prune juice, or is rusty. This stage usually lasts 24 to 48 hours (see under icterus—gall bladder—in reference to icterus in pneumonia).

(*b*) **Hepatization.**—Fibrin formation steadily increases, and loose and dense net-works of fibrin threads appear (fig. 181). The fluid congeals into a solid mass and the consistency of the lung becomes firmer, like a liver. In the beginning, the color of the section surface is red to grayish red (more pale than in *a*).

The vessels are still markedly filled and the exudate shows many red and white blood corpuscles, as well as exfoliated, swollen, lumpy, granular, poorly staining epithelial cells, mostly without recognizable nuclei (red hepatization).

If the blood is washed off with water, the color becomes lighter gray, since the color of the fibrin is made more prominent.

To obtain a true conception of the quantity of fibrin, it is necessary to use Weigert's staining method (not strictly specific), after celloidin embedding. E. Fraenkel advises the use of Best's carmine stain, usually used for staining glycogen. Fibrin stains deep blue violet. The pneumococci are also stained blue violet, and their capsules, if carmine is used previously, are red in color. In such preparations, the fibrin is usually found most abundant in the peripheral parts of the alveolar plugs, but fine fibrin bundles pass through the spaces or "pore canaliculi" which were first observed in pneumonia, extending from one alveolus to another (see p. 338). Fibrin threads and larger fibrin masses are also found in

the lymph vessels, and fibrinous thrombi in the larger and smaller blood vessels. Sometimes whole systems of capillaries are as if artificially injected.

The pneumococci are found most abundantly, and with highest virulence at the beginning of hepatization (Welch); they are often located in leucocytes. The mass of the latter in relation to the fibrin varies considerably in different alveoli; sometimes the bronchioles and infundibuli contain almost nothing but leucocytes (macroscopic yellowish foci) and abundant cocci, while fibrin predominates in the alveoli, and cocci are absent. The co-existence of cocci and leucocytes, which is also seen in other situations,

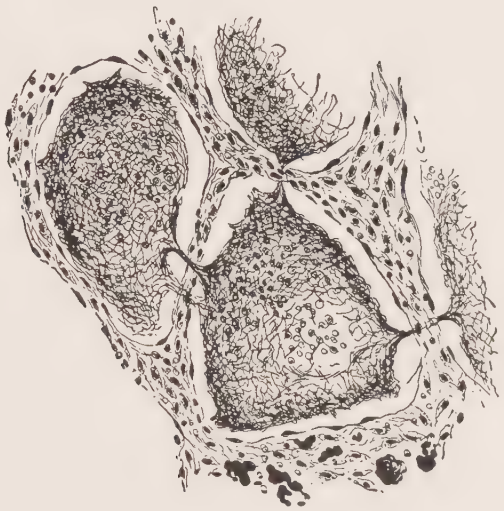


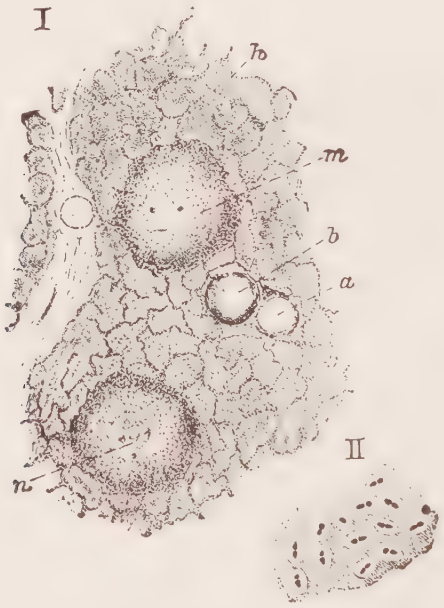
FIG. 181.—Fibrinous pneumonia. Weigert's fibrin stain. (The black felted fibres are blue violet.) Between the alveolar plugs are bridges of thready fibrin bundles penetrating the alveolar walls (pore-canaliculi). Below in interstitial tissue much coal pigment; (high power).

is interpreted as a chemotactic action of the microorganisms (*i.e.*, of their toxins) stimulating leucocytic collection.

The remarkably heavy lung, voluminous to the extent of its maximum inspiratory size, is devoid of air in its affected portions.

The alveolar granulation mentioned above (p. 388) is quite plain on the section surface, especially on a fracture surface. Should the lung be emphysematous, the granules are much larger. They can be scraped off with a somewhat cloudy sanguinous fluid and represent casts of the alveoli, infundibuli and bronchioles. They are quite solid and firm, and may remain so at the beginning of gray hepatization. Later, they soften in proportion to the progression toward light gray to grayish yellow hepatization, and the leucocytes steadily increase in the exudate.

From its grayish red hepatization which rarely lasts longer than three or four days, the pneumonia then passes on to resolution (*c*), or from the gray, almost unchanged, firm, granular hepatization, it progresses to grayish yellow hepatization which gradually becomes lighter in color. In the latter stage, the tissue is very heavy, and one lung may weigh 1.5 to 2 kgs. or more, indeed, as the author observed, one lower lobe weighed 2 kgs; it is less firm, extremely friable, and still more voluminous than previously. The lungs do not collapse when the thorax is opened, but remain firmly pressed against the thoracic wall so that the impressions of the ribs show on their surface.




FIGS. 182 and 183.—I. Gray hepatisation of lung; accidental combination with miliary tuberculosis; mm, miliary tubercle; a, artery; b, bronchus containing exudate; h, hepatized areas. II. Pneumococcus (Frankel-Weichselbaum). Diplococci with capsules from lung fluid. Gram stain. Oil immersion.

If several lobes are affected the lung bulges outward when the sternum is removed. If there is marked anthracosis, it has a marbled or granite-like, veined appearance. The alveolar granulations are diffused, and a thick paste can be scraped off by the knife.

Microscopically, little or no blood is visible in the gray red hepatization, the exudate being characterized by enormous numbers of leucocytes, some of which stain poorly, and many of which contain fat granules; the fibrin diminishes in amount, becomes granular and amorphous or clumped into shiny masses showing no network. The leucocytes give the exudate an

appearance almost like that of pus and are derived from the capillaries and veins since their blood contains many of these cells (leucocytosis, see p. 198).

Since the alveoli are filled to the maximum, they press against each other and on the vessels. This circumstance, in combination with the fibrinous thrombi in some blood vessels (mentioned p. 392), contributes to impairment, although not complete interruption, of the circulation with a resulting pale color of the parts. That the subsequent regressive changes (*c*) in the exudate depend partly on this, is not probable; it must rather be assumed that death of the pneumococci allows resolution of the exudate by the increase of leucocytes.

(*c*) **Resolution** (Lysis).—The exudate softens and finally disintegrates into an emulsion. The color of the section surface is diffusely greenish yellow to yellow, and shows dark red spots. The consistency of the lobe, still airless, becomes softer; the granules have disappeared. The section surface grows more moist and a turbid, smeary, shiny, puriform substance, at the beginning grayish yellow, later, creamy yellow, flows off. The tissue is heavy, soft, and still more friable than in gray hepatization, due to the fragility of the elastic elements, which, as a rule, soon disappears after the pneumonia is over (see below).

If the soft, moist, fragile lung tissue is handled carelessly, the pressure of the fingers crushes areas and forms "pseudo abscesses," *i.e.*, cavities filled with softened exudate (comp. p. 400).

Disintegration of the exudate and its dominant cells, leucocytes, can be seen microscopically. Macrophages, three to four times the size of leucocytes and containing granules of disintegrated fibrin, are also seen (comp. Milian).

The slimy consistency is due to fibrin liquefaction (Fr. Muller); the leucocytes, as in other purulent liquefactive processes, supply the digestive ferment (proteolytic enzyme). The cells in the exudate undergo fatty degeneration, supplying the yellow color and the moist, slimy, creamy appearance of the section surface.

It must be especially emphasized that the puriform fluid of the stage of resolution is not pus, but an emulsion of liquefied exudate and cells undergoing fatty degeneration.

Pneumococci gradually disappear, generally with the beginning of the crisis, but they can be demonstrated for a long time in the sputum, even after convalescence.

Clinically, as a rule, the crisis coincides with resolution (sudden drop of fever, copious sweats, feeling of well being) and the urine shows marked sedimentation. The leucocytosis of the blood, chiefly polymorphonuclear, also drops suddenly.

Only a small part of the emulsified exudate is removed by expectoration (turbid sputum); the largest part is eliminated with astonishing rapidity by absorption through the lymphatics. The alveolar epithelium regenerates and there is complete recovery.

The lung regains its air in approximately 14 days, but remains vascular, less elastic, fragile and easily torn, until about the fourth week.

Duration of pneumonia: Pneumonia usually runs a course of one to two weeks, but cases occur of shorter and longer durations in which the regular stages are less completely or more swiftly developed, or protracted. This depends not alone on the susceptibility of the patient, but also on the biological properties and virulence of the infecting microorganisms. The older the patient, the more severe the disease. The completed red hepatization usually takes from three to five days, the gray to grayish yellow hepatization from six to eight days; but these calculations are only approximately correct. Death may occur at any stage; in about one-third of the cases it occurs from cardiac insufficiency during the stage of gray hepatization, if resolution and crisis—usually appearing on the seventh day—are delayed.

Most patients die on the tenth to twelfth day, and it is clear that, considering the factor of delayed course, it is impossible to deduce with certainty the duration of the disease from the anatomical picture. Some assume that bacterial toxins bring about death through vaso motor paralysis. Removal of the function of the respiratory parenchyma alone is but seldom a cause of death.

**Locality. Extension. Atypical Forms.**—The right lung is more frequently involved than the left. In either lung, the lower lobe is preferred. If several lobes are affected,—in rare cases, all are involved,—several stages appear simultaneously; in fact this has often been observed in one lobe. For instance, the transition of one stage into the other may develop thus: the lowest segment shows marked gray hepatization, the middle portion grayish red, and the uppermost congestion, but the several segments usually fuse into each other. The designation is selected according to the predominant stage. If pneumonia extends by continuity, step by step, from one place to another, the clinician speaks of "pneumonia migrans." If it extends in jumps, it is called "erratic pneumonia." In central pneumonia, the disease begins at the hilum (bronchogenous, see Hesse, lit.) and progresses further, without touching the periphery. In children, it is commonly a lobular type, even in pneumococcic pneumonia, and is rarely a typically lobar pneumonia. So-called soft pneumonia (serous) is characterized by less fibrin in the exudate, and so there is absence to a great extent of the typical granulation of the section surface, the infiltration, corresponding to the inflammatory edema, is more serous,

and flabby, and air displacement not as complete. This type is often seen in aged and decrepit individuals.

In the early stages of pneumonia due to bacillus capsulatus (p. 389), the exudate is slippery, slimy, less sanguinous, and contains more swollen epithelium; in later stages, the leucocytes are much larger than those in diplococcic pneumonia on account of vacuoles which contain bacilli Kokawa, lit.). According to Apelt, the course is especially severe. In that due to the streptococcus mucosus (p. 389), the exudate on the pleura is also slimy and sticky (see Haas).

Flabby pneumonia may also be due to influenza. But the relatively frequent lobar influenza pneumonia, in which streptococci, more rarely pneumococci and staphylococci, occur in conjunction with influenza bacilli, is, as a rule, typically granular and croupous; it differs from pure lobar pneumonia chiefly in the presence of a diffuse purulent bronchitis, even in healthy parts (Kundrat, Paltauf; see p. 402).

The hemorrhagic form of fibrinous pneumonia is rare.

It is of some medico-legal importance, as v. Hofmann emphasized, and Heller pointed out, that cases occur, especially in aged individuals apparently in the best of health, in whom autopsy shows pneumonia in some stage when the death was quite sudden.

Pleuritis over the hepatized portion is a constant accompaniment. The pleura, bluish violet, cloudy in color, shows a rather small amount of dry fibrinous coating (pleuritis sicca), but this condition is changeable, and the exudate may be serofibrinous or rich in pus cells and even actually purulent, although this is exceptional.

Fibrinous pleuritis heals by resolution of the exudate or by organization with thickening and perhaps actual fibrous adhesions of the pleural surfaces, especially over the lower lobe. On the other hand, Schridde considers such adhesions (also traumatic) responsible for the development and localization of pneumonia.

Likewise, the bronchi are always involved. The smallest show fibrinous, cellular exudates. Small fibrin casts are very frequent and can be pulled out with forceps. Larger bronchi usually show only a catarrhal inflammation, but sometimes occluding, branching, fibrin coagula extend upward into them (massive pneumonia, Grancher).

Such a fibrinous exudate is not derived essentially from the bronchi themselves (epithelium is preserved), but from the alveoli, *i.e.*, infundibuli.

Hemorrhagic fibrinous bronchitis is rare.

The lymph vessels of the lung and the bronchial lymph nodes are always involved in pneumonia, although to varying degrees. This is related in part to absorptive activity, but also in part to active participation in the inflammatory process. For instance, the swelling and redness

of the bronchial nodes due to absorbed red blood corpuscles in the congestive stage, as well as other contents, point to increased absorption. Then, as the progressive hepatization impedes absorption, there is corresponding possible regression of the lymph nodes; the marked swelling and moisture beginning at the time of resolution indicates active absorption again.

As a rule, lymphangitis and perilymphangitis within the lung are related to absorption of the causative organisms from the diseased parts and may appear before resolution. Usually, they are only recognizable microscopically as cellular infiltrations in the vicinity of lymph vessels, the lumena of which are filled with fibrinous masses (fibrin stain). Sometimes, however, net-like, branching lymph vessels can be seen macroscopically in the pleura, often beautifully arranged in relation to the interlobular septa; they are broad and filled with light gray material, as a true lymphangitis, *i.e.*, perilymphangitis with lymph thrombosis. An interstitial pneumonia is added to the alveolar pneumonia. When numerous interstitial lymphatics are destroyed as in emphysema or in pathological apices, pneumonic exudates tend to remain unabsorbed.

### UNUSUAL ENDING OF LOBAR PNEUMONIA

**Carnification, Chronic Fibrous Pneumonia, Induration.**—When the fibrino-cellular exudate remains in the alveoli, resolution does not take place, at times, for unknown reasons, in both pneumococcic and streptococcic pneumonias; active productive inflammation in the lung tissue produces vascular young connective tissue which penetrates the homogeneous and clumped exudate and organizes it. In the course of weeks, the hepatized area becomes an airless, moist, red to brownish red, or grayish red to gray and mottled tissue, dotted with fine, pale yellow or almost white spots; the tissue is glassy, and of tough consistency.

Absorption occurs, however, and is not entirely absent as it is when the lymphatics are atrophic from preceding pneumonias (Hart) or pleural adhesions (Marchand); the decisive factor is that resolution does not occur. The fibrin stimulates the tissue to productive inflammation.

This change may involve the greatest part of a lobe, but, ordinarily, it is confined to a smaller subpleural area, or to a strip between air-containing tissues.

Microscopically, extensive proliferation of pulmonary connective tissue is seen, especially rich in spindle cells, but also containing round cells. Accompanied by numerous young blood vessels, it penetrates the exudate which undergoes much fatty degeneration (leucocytes, desquamated epithelium). A doubly refracting, fat-like substance appears in macroscopically yellowish white places, but perhaps also in areas brown from altered blood pigment (see pp. 377 and 408).

Cellular proliferation extends through the pore canaliculi from one alveolus to another using the contained fibrin fibrillae as guides (fig. 184). Sometimes plugs of polypoid granular tissue extend into the alveoli and the small bronchi. The connective tissue proliferation starts not only in the alveoli and their walls (v. Kahlden) which are thickened and more cellular, but also in the connective tissue around the terminal bronchi and alveolar ducts, and the perivascular, interlobular, and pleural connective tissues. The adhesive proliferating mass fills not only the alveoli, ducts, and terminal bronchi, but also thickens the interstitial tissue. Ribbert, Hart and others believe the proliferation begins in the

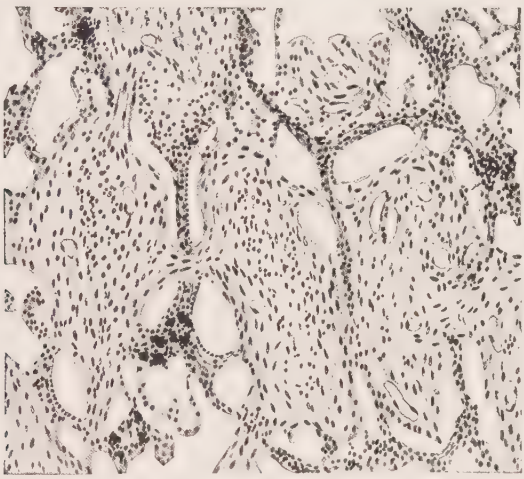


FIG. 184.—Carnification of lung; 5 weeks old stubborn pneumonia. Alveoli filled with vascular connective tissue plugs which adhere to the cellular walls and communicate with each other through the dilated pore-canaliculi; (med. magn.).

bronchi and progresses downward into the alveoli. Abundant vascularization is very necessary, and pleural adhesions may be of importance in establishing numerous anastomoses (Marchand). For some reason, certain alveolar, cleft-like spaces are not included in the proliferation. During this time, the alveolar epithelium proliferates, desquamates, and partly covers the intra-alveolar connective tissue with the help of the bronchial epithelium (Mello). The cells become cubical to cylindrical, and, especially in older cases, produce irregular gland-like proliferations, giving, perhaps, the impression of a tumor such as a beginning adenocarcinoma. It is considered an attempt at regeneration. Giant cells are frequent.

Nothing remains where the alveoli are completely obliterated, but a focus of connective tissue without pulmonary architecture.

Not rarely, the calloused parts contain many corpora amylacea (p. 372).

In sections of lungs which looked macroscopically like common carnification, the author saw pictures analogous to the muscular cirrhosis described by Davidsohn; the starting point of muscle fiber strands from small bronchi could be plainly demonstrated. Buhl and Eberth-Pepere have also described this condition, Eberth in siderosis, and Tanaka saw it in syphilitic lungs (comp. Baltisberger, lit.).

Carnification is also fairly frequent in tuberculous lungs, in tuberculous (caseous) pneumonia, etc., (see there, comp. Ceelen).

The older the proliferative process, the greater the change to firm, contracting connective tissue confined to isolated foci or strands, or diffused over large areas. It is called induration, contraction, cirrhosis, or inflammatory obliteration of the lung. Pleuritic adhesions and bronchiectasias are frequently present in the indurated areas (see p. 353).

**Purulent Pneumonia—Abscess Formation.**—Pyogenic organisms may lead to suppuration, purulent liquefaction, or abscess formation. The organisms may have been the cause of the pneumonia; indeed in rare cases they may be the pneumococcus itself, or secondary organisms are added. In drinkers, purulent pneumonia is more common. Focal soft areas, mostly multiple, yield creamy, viscid pus on compression. The lung tissue is liquefied; after the pus is washed out, holes with irregular, ragged walls remain in the hepatized lung tissue. Sometimes cholesterin and hematoidin crystals appear in the sputum. (See p. 395 as to artefacts—pseudo abscesses—purulent pneumonia in influenza, pp. 341 and 403.)

**Gangrene.**—When the organisms of decay are given free rein in the exudate (as in purulent bronchitis), bronchiectasia, purulent necrosis and gangrene occur. The tissue is discolored and fetid. This occurs mostly in old, decrepit individuals, in diabetics, relatively often in drinkers; as a whole, the complication is infrequent.

A rare event is for the pneumonic tissue to undergo focal necrosis because of insufficient nutrition from vascular occlusions, such as stasis, or thrombosis; anemic, non-purulent "infarcts" appear. According to Apelt, this is especially frequent in bacillus capsulatus pneumonia, a statement verified by the author. Suppuration may spread in the vicinity and large masses of dead tissue become sequestrae (lit. by Rosenthal).

**Translator's Remarks.** For studies of the toxicity of pneumonic lungs, the properties of pneumotoxin, etc., see Weiss, C. J. Med. Res. 39: 103: 1918. Arch. Int. Med. 23: 395: 1919. Weiss, C., Kolmer, J. A., Steinfield, E., J. Infect. Dis. 22: 469: 1918. See "Pneumonia at a Base Hospital," Cole, R. and Mac Callum, W. G., J. A. M. A. 70: 1146: 1918. For clinical and bacteriologic

studies, see Cecil, R. L. and Larsen, N. P., J. A. M. A. 79: 343: 1922. For experimental pneumonia in rabbits and lit., see Permar, H. H., J. Med. Res. 44: 1: 1923 and page 27 of same vol.

**Bronchopneumonia—Bronchogenous Focal Pneumonia.**—Bronchopneumonia is decidedly different from lobar, true pneumonia. It is a form of bronchogenous pulmonary inflammation consisting of more or less numerous small foci (bronchogenous focal pneumonia) in lobular or peribronchial arrangement. When the foci are continuations of primary disease of the smaller bronchi, it is spoken of as bronchopneumonia in the narrower sense.

The contrast between lobar, and lobular pneumonia is, however, not essential (anatomically). When lobular foci become confluent as they do so often in children, the picture is similar to the lobar form, but in other parts, are usually scattered foci. On the other hand, primary lobar pneumonia, as mentioned on p. 389, often enough shows indications of lobular composition, or, at least, dominant centers can be recognized (p. 389); scattered foci are usually absent.

Two groups of bronchopneumonia can be considered:

(*a*) Inflammation progresses down the lumen of the bronchus to the alveolar parenchyma, or an exudate is aspirated from the bronchi into the alveoli. In other cases, inflammatory causes, *e.g.*, gases, reach the infundibuli and alveoli directly by way of the bronchi and cause inflammatory foci of varying size. Sudden inflammations of the bronchi and their respective respiratory parenchymas also produce foci first occupying the centers of lobules. Since deleterious substances can be inhaled or aspirated by way of the bronchi, *i.e.*, from its lumen, these are spoken of as inhalation—or aspiration pneumonias in given cases (forms of bronchogenous focal pneumonia).

Thus, as far as they are bronchopneumonias in a narrower sense, the qualifying clause may be added, "with endobronchial extension." In short, this type is spoken of as lobular pneumonia.

(*b*) But there is another route of propagation of inflammation from the bronchi to the alveoli especially frequent in children with the exanthematous infectious diseases (mentioned on pp. 347 and 348). First an (endo-) bronchitis develops, the bronchial wall and the peribronchial tissue become involved (peribronchitis), then the inflammatory infiltration extends into the intraalveolar septa, and with these as guides, it creeps in various directions toward bordering alveoli, which naturally do not, for the greatest part, belong to the actual respiratory extension area (lobulus) of the affected bronchus, but to the systems of other bronchi. Thus, various sized, rounded, or oblong, infiltration foci are developed

around a diseased bronchus. They are best called peribronchial (alveolar pneumonia), *i.e.*, focal bronchogenous pneumonias, and not lobular bronchopneumonias (fig. 168, comp. p. 348). But peribronchial focal pneumonias may also be called bronchopneumonias by peribronchial extension (*b*); (*a*) and (*b*) are frequently combined.

It follows from what has been said, that bronchopneumonia does not have uniform anatomic characteristics but varies with the kind of bronchitis, or with the kind of injurious substance which reaches the alveoli by inhalation or aspiration.

But, bronchopneumonias have in common, (1) their relation to the bronchial tract, (2) the formation of distinct foci, which, however, may become confluent, and vary greatly in appearance, numbers, density of groups and the manner in which they affect both lungs simultaneously or successively.

The lobular arrangement is most easily recognized when the inflammation involves isolated bronchial branches, and other areas are intact. The very distinct bronchopneumonic foci are then prominent on the section surface. They are, generally speaking, less granular than the consolidations of true pneumonia and are grayish red; later, fatty degeneration of the exudate increases the yellowish, sulphur yellow, or whitish gray colors. Usually, the exudate may be pressed out in droplets.

When a large part of the bronchial tree and its parenchyma is flooded by some irritant fluid (aspiration pneumonia), the inflammatory infiltration is obviously diffuse. But even in such cases, the infiltration can usually be differentiated from that of true pneumonia because it is less regular, and encircles more or less air-containing lobules, while discrete foci are usually present in other places.

The exudate in bronchopneumonia varies from simple catarrhal, hemorrhagic, fibrinous, purulent to gangrenous.

Purulent and gangrenous bronchopneumonia, at the beginning an internal surface affection, leads very quickly to active involvement of the surrounding interstitial tissue and thus to disintegration of the focus, suppuration of the lung, and gangrene (comp. p. 409).

If the exudate corresponds to that of a simple bronchial catarrh, it is called catarrhal bronchopneumonia. It contains much albumen but usually does not coagulate, and can be squeezed out in drops. Its cells are desquamating alveolar epithelium sometimes in adhering plates or tags, and immigrated leucocytes. Increase of the latter causes the exudate to become more purulent. Desquamated alveolar epithelium swells into rounded cells which show fatty and granular degeneration. The exudate fills the alveoli more or less completely, while the interstitial tissue is hyperemic and infiltrated with round cells (see fig. 185).

The relative masses of cells and fibrin vary; frequently, very little or none of the latter is present; in other cases the quantity is so considerable that it leads to true alveolar granulation, as particularly in laryngeal diphtheria and measles in children, in whom otherwise the lobar fibrinous pneumonia of adults hardly ever occurs.

According to Kromayer and Durck, the pneumonias of diphtheria and measles are apt to show the formation of giant cells from epithelium in alveoli which do not contain their full complement of air (see also Honl, Steinhaus and Hart, Hecht, Ribbert and comp. p. 342). This has been observed by the author in pertussis as well as in other bronchopneumonias, while Hecht produced experimental giant cell pneumonia in rabbits by using diluted metallic salt solution. See Watjen in reference to plasma cell infiltration, especially around the small bronchi in the pneumonias of children (diphtheria, pertussis, measles).

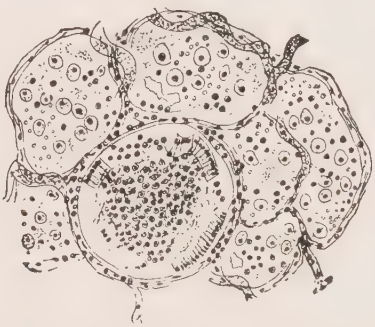


FIG. 185.—Catarrhal bronchopneumonia. Small bronchus, fluid contains many leucocytes. Alveoli filled with finely granular coagulated exudate, sparse white and red blood corpuscles and numerous desquamated rounded epithelial cells; (medium magn.).

There are cases in which the exudate has a hemorrhagic character, (hemorrhagic bronchopneumonia), *e.g.*, in scarlet fever, diphtheria and influenza.

According to Finkler, splenization of foci is more frequent than hepatization in streptococcic pneumonia; the tendency to progress and to cellular infiltration of the interstitial tissue resembles erysipelatous inflammation. Influenza pneumonias show similar characters, but generally speaking, there is a tendency to grave consequences such as suppuration, purulent lymphangitis, interstitial suppuration, necrosis in irregular foci and gangrene. The picture of red or gray or grayish yellow hepatized foci may be obscured by hemorrhages (spoken of as "colored" lung), and furthermore, purulent pleuritis, pericarditis, peritonitis, etc. are common (Kundrat, Paltauf, also Simmonds, Schoppler, Scharer, lit. and many more). Compare influenza under bronchi, p. 341, and croupous pneumonia, page 397, also pneumonia purulenta dissecans, p. 415.

**Pathogenesis. Etiology.**—Bronchopneumonias often develop in atelectatic areas, edematous from some cause or other. Conversely, when the secretions of a catarrhal bronchopneumonia block the bronchial lumena, atelectasis may develop. In like manner, a bronchogenous catarrhal pneumonia may supersede hypostasis (p. 374), so that the alveolar contents are cloudy, sanguino-watery, and at times rich in cells or fibrin, when the focus is found to be granular.

In such cases we may conceive the development of the inflammation in this manner: pathogenic bacteria are present in the upper respiratory tract of the healthy (Besser), and by inhalation or successive aspiration from without or from the upper tracts (nose—in rhinitis;—tonsils) pass downward where ordinarily the mechanical and chemical protective apparatus of the lungs (see below) removes them or makes them harmless (comp. Nenninger, Quensel, Wrzosek). If conditions are changed and they are offered favorable environment, they produce inflammatory reaction. This applies to the staphylococcus, streptococcus pyogenes, pneumococcus, the pneumobacillus of Friedlander, influenza bacillus, and also to a mixture of pyogenic organisms. Non-pathogenic bacteria are also found.

It is presumed that the mere presence of these bacteria does not usually suffice to produce a pneumonia, but that a predisposing cause is necessary, *e.g.*, dust, gases, heat in burns (B. Fischer and Goldschmidt), colds, etc. This idea is supported by the experimental experiences of Durck and Muller, who showed that bacteria which enter the healthy lungs in respiration are carried off by leucocytes, destroyed by phagocytes and killed by bactericidal organ juices (Paul), or are rendered sufficiently avirulent so that the majority can develop only in suitable pabulum (*i.e.*, fluid), and thus can only be demonstrated culturally.

Thus can be partly explained the so-called germ-free lungs of other authors (Fr. Muller and others) who worked with solid culture media; but bacteria need not be present in every small piece, or even in every lung. A good resume of this question can be found written by Fr. Muller, criticism by v. Baumgarten who believes the normal lung is germ-free, (Ad. Schmidt). The part played by "catching a cold" from local or general exposure may possibly be explained in this wise: from circulatory disturbances the bactericidal protective substances of the lung tissue are diminished (A. Wassermann), so that bacteria, until then held in check, can rapidly increase, become aggressive, infectious, and penetrate the tissues (auto infection). While such a condition is probably quite frequent, very virulent bacteria, on the other hand, may cause pneumonia directly by transportation into the intact, deep air channels. Then the action of cold is not a necessary factor.

Bronchopneumonias develop very often in children in conjunction with the bronchitis and bronchiolitis of various infectious diseases, particularly measles, in which most of the fatalities are due to bronchopneumonia, scarlet fever, diphtheria, influenza, pertussis. A peribronchial extension is practically always present, sometimes with a well defined descending endobronchitis as well. The posterior and lower lung segments are the favorite sites. In other severe infections, also, such as typhoid fever and small pox, bronchopneumonia may appear.

In all these diseases, however, the pulmonary inflammation is probably not due to the specific bacteria of the special infection, but to common pathogenic organisms so frequently present in the respiratory tract. Among these are pneumococci in one half of all cases of bronchopneumonia (Netter), streptococci, staphylococci, pure or frequently in mixed cultures. Thus it is a secondary infection favored by the primary disease (measles, typhoid, etc.). In the bronchopneumonia of influenza, not only is the influenza bacillus present (p. 341), but also the pneumococcus, streptococcus and staphylococcus. There are, however, pure cases of specific infection such as the bronchopneumonia of the diphtheria bacillus or of the influenza bacillus. More rarely, colon bacilli have been found, which possibly reached the lungs by the hematogenous route from the intestines (Sevestre), or from inflammatory processes in the urogenital tract, an idea which has been disputed by Spiegelberg and others, who believe in the "most natural route," *i.e.*, the bronchi. Some French investigators accept the possibility of an hematogenous bronchopneumonia in certain cases such as those following skin suppurations (impetigo, etc.), (comp. Milian). v. Baumgarten cautions against overrating the lung as a portal of entry for infectious microorganisms.

Rare specific forms of pneumonia must be mentioned:

1. Anthrax pneumonia or so-called "rag-picker's disease" (Eppinger, Paltauf), which follows the inhalation of spore-infected dust, or perhaps a hematogenous infection with portal of entry in the mucosa of the upper respiratory tract (comp. v. Baumgarten) is sometimes observed in persons occupied in sorting rags in paper mills. Edema and infiltration of the lungs take place in lobular, or even lobar distribution with an exudate sometimes sanguinous. Extension occurs in the pulmonary lymph vessels and propagation to the pleura with subsequent sero-sanguinous exudation into the pleural cavity. The mediastinal connective tissue and the mediastinal and bronchial lymph nodes are also involved. The nodes undergo sero-sanguinous swelling; the moisture of the mediastinum with its swollen hemorrhagic nodes is noticeable as soon as the sternum is removed, and this may be a valuable hint during autopsy. Bacilli are

found especially in the dilated pleural and pulmonary lymph vessels, but also appear in the other places mentioned.

2. Pest pneumonia is one of the three clinical forms of bubonic plague (comp. p. 253), very serious in its course, unfavorable prognostically and extremely infectious to the surroundings. Plague patients have been known to cough up bacilli seventy-six days after recovery (Gotschlich).

Pest pneumonia may develop primarily as a confluent lobular affair by way of a bronchitis due to inhalation of the plague virus, or by aspiration from necrosing inflammatory lesions in the mouth or pharynx, or as an embolic metastatic form in which the foci are multiple and peripheral with preference for the lower lobes (H. Albrecht and Ghon). The foci, distinguished by necroses of septa and vessel walls and slight homogeneous exudation without fibrin, contain bacillus pestis in enormous numbers. By the combined activity of pest bacilli and other bacteria (pneumococci, influenza bacilli, streptococci and tubercle bacilli), necrotic destruction and hemorrhages in the lungs occur (hemorrhagic pneumonia). In the middle ages, the expulsion of black masses and hemophages was called "black death" (comp. Frosch), but according to Marc, this name was given to subcutaneous hemorrhages. Durck considers primary plague pneumonia very rare; the primary focus may be relatively unimportant and the dominant clinical pneumonia is easily mistaken for a primary lesion; plague bronchitis, on the other hand, is supposed to be quite frequent.

3. Psittacosis (Leichtenstern) is an atypical pneumonia usually in the lower lobe, giving symptoms of typhoid fever and probably due to transmission of a disease of parrots. It is a specific infection in man, appeared first in Paris in 1892, was epidemic, usually as a house epidemic with a high mortality. Nocara at that time described a bacillus resembling bacillus typhosis, but differing in certain respects.

In severe infections, and other diseases accompanied by unconsciousness, or requiring the recumbent position for a long time and from anesthesia also (ether, etc., Nauwerck, Holscher), bronchopneumonias occur by aspiration of mucus and bacteria from the upper tracts, especially from the buccal cavity, or from swallowing. Secretion is stimulated by the ether in the bronchi, and with the transudate from the pulmonary capillaries (Lindemann), supplies a good culture medium. Such inflammatory foci often undergo suppuration and necrosis (comp. p. 409).

Klipstein demonstrated experimentally the downward progress of bacteria from the naso-pharynx into the lung.

In aspiration pneumonias, Kreibich found the pneumococcus alone, in half of the cases, and mixed with other bacteria in the other cases.

Quite a number of poisonous gases, or dusts, or fluid substances cause severe bronchopneumonia. Some have been mentioned under obliterat-

ing bronchitis (p. 342), to which list may be added illuminating gas, nitric acid (comp. Loeschke), sulphuretted hydrogen, Thomas' phosphate flour. In a pneumonia due to the last named substance, Enderlen found pneumococci.

In the aged, a fatal catarrhal bronchopneumonia is very frequently added to a bronchial catarrh.

A lung with lobular bronchopneumonic foci is apt to be variegated and marbled, especially in children, in whom atelectasis from bronchial

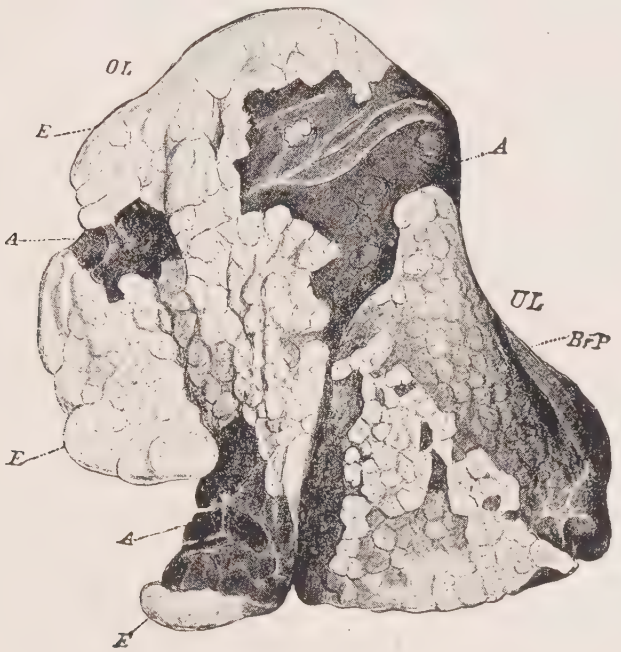



FIG. 186.—Left lung of a child who died of a pseudomembranous inflammation of larynx, trachea and bronchopneumonia. OL, upper lobe; UL, lower lobe; between is the dark interlobular cleft; A, atelectases dark blue deeply situated; E, acute vesicular emphysema. The puffy sections are very pale, markedly projecting, causing the sharp edge to become rounded with irregular lumpy outline. BrP, Lobular bronchopneumonia, flat humped, projecting, firm. $\frac{4}{5}$ nat. size, drawn from fresh specimen.

obstruction as well as complementary emphysema are usually developed. Most foci are situated in the lower lobe.

Fig. 186 will serve as an illustration. In the lower lobe (r.l.) are numerous bronchopneumonic foci, slightly bulging in the form of knobby lobular fields; according to the stage, they are dark blue red, red, gray to yellow in color, and of firm consistency (bronchopneumonia). Isolated bronchopneumonic foci are present in the upper lobe, in a large dark field, directly above the interlobar fissure, also between the emphysematous pale lingula and the dark atelectatic area (*a*), and between this and the dark field situated above, which is sharply circumscribed, atelectatic and

of lobular architecture (*a*). The sharp edge of the lung is partly emphysematous and partly atelectatic, so that its outline is extremely irregular. The other lung was quite similar in appearance.

The pleura is usually covered by a thin veil of fibrin.

The section surface shows quite similar marbling. The lobular foci are airless, of varying sizes from that of a pinhead to coarse nodules, somewhat prominent, slightly granular, grayish red to yellowish gray (regressing), and the centers are somewhat lighter in color than the peripheries; they are especially prominent between atelectatic, deep bluish red, smooth, glassy tissue. Even when closely packed, the lobular structure is easily recognized. A tough, turbid, yellowish gray fluid can be expressed in drops. Air-containing parts of the lung are a cinnabar color, or, if emphysematous, pale red to yellow white.

**End Results of Catarrhal and Fibrinous Bronchopneumonia.**—Healing. During resolution, usually after some weeks, the exudate disintegrates into a poultaceous mass partly fatty; some is expectorated, but the larger proportion is removed by lymphatic absorption.

Death is frequent in children and the aged, even with mild extension (see pp. 403 and 407).

Later infection may soften simple pneumonic catarrhal foci into suppurative and gangrenous masses.

Chronic Catarrhal Pneumonia.—As the catarrh becomes chronic, the exudate grows more viscid; the cells undergo fatty degeneration and the fat granules are taken up by cells (fat granule cells). Sulphur yellow spots then appear on a glassy, gelatinous, gray background and may be mistaken for gelatinous caseous pneumonia. It has been emphasized that this material is not true fat, but a doubly refracting substance. Furthermore, according to Rindfleisch, it is not a catarrhal inflammation, but an old edema which followed atelectasis (see p. 378). The alveolar epithelium may grow atypically (comp. p. 399) while the interstitial tissue proliferates and slowly leads to cicatricial induration; many blood vessels are obliterated.

Chronic fibrinous bronchopneumonia sometimes appears as small, later quite cicatricial, gray peribronchial nodules within which bronchiectasia may develop. It has been mistaken for healed tuberculosis (comp. fibrous obliterating bronchiolitis, p. 342).

Caseation of the exudate of catarrhal pneumonia and the appearance of tubercles in the pneumonic portions are occasionally observed in scrofulous children, who die after a long illness of scarlet fever or measles; according to Kromayer and Koster, a peribronchitis and peribronchial pneumonia of the extreme ends of the bronchi are characteristic. Old tuberculous processes in the lungs are found, or more often, old caseous

bronchial nodes with an older pulmonary affection, but sometimes indeed tuberculosis of the lungs is entirely absent. The pulmonary foci of the acute infection (measles, pertussis) are invaded by tubercle bacilli carried from caseous lymph nodes presumably by the increased lymph and blood circulations. But perhaps in some cases the bronchioles, predisposed by measles, are infected by the fresh aerogenous advent of tubercle bacilli (Koster). This leads to diffuse caseation, or to the formation of numerous miliary tubercles.

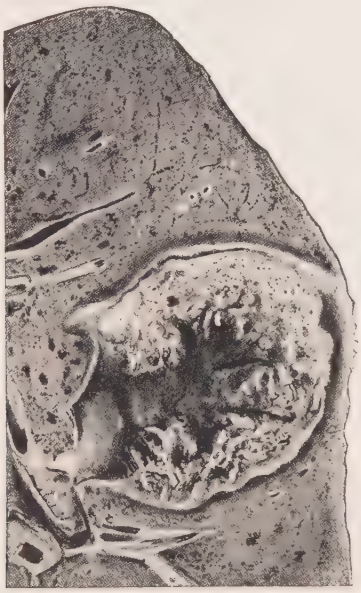


FIG. 187.—Gangrenous area in l. lower lobe of man 78 years old; the cavity is surrounded by a light area of fatty degeneration. 5/6 nat. size.

In fact, in conjunction with catarrhal pneumonia, so many tubercle bacilli from caseous lymph nodes may enter the blood and lymph channels that a general miliary tuberculosis results.

3. Inflammations causing abscesses (suppurative liquefaction) and gangrene (purulent decomposition).

In contrast to the catarrhal and fibrinous (croupous) inflammations localized chiefly to the interior of the alveoli, *i.e.*, to the so-called alveolar surfaces, purulent and gangrenous inflammations destroy parenchyma and produce cavities which may heal by cicatricial atrophy, or leave smooth walled spaces if the contents are expelled.

It has been stated above (p. 406) that some bronchopneumonias with suppuration and necrosis develop from aspiration through the bronchi, but there are other possible sources. The most important are septic

emboli which establish purulent and gangrenous metastatic focal pneumonias (also called metastatic abscesses and gangrene).

What is called "circumscribed suppuration," *i.e.*, abscess, and what is called circumscribed gangrene differ from diffuse suppuration (purulent pneumonia), and diffuse, so-called lobar, gangrene. The latter is usually confluent gangrenous bronchopneumonia with putrid bronchitis, and in its chronic forms is extremely complicated (p. 412).

The following description is of fully developed foci. A pulmonary abscess in this stage is a cavity filled with creamy, yellowish green, usually odorless pus (although it may have a foul odor) with the walls infiltrated by pus cells.

An early gangrenous focus consists of a discolored, grayish green to blackish brown mass emitting a penetrating, offensive odor; as liquefaction progresses, it becomes a stinking, ichorous, gangrenous, rough walled cavity, with a tendency to bleeding (fig. 187). The black discoloration around the focus is due to a combination of the iron-containing pigment, hemosiderin, liberated from red blood cells, and decomposition products containing sulphuretted hydrogen. Although typical abscesses and gangrenous foci are quite different in appearance, yet many combinations occur of both.

Globular or rounded, discrete cavities, occasionally in larger numbers, are more likely to be metastatic (embolic), while more irregular cavity systems, corresponding somewhat to wedge-shaped bronchial areas, are aerogenous, bronchogenous abscesses, and gangrenous foci.

Microscopically, are found pus cells, lung fragments, elastic fibers, and, according to the case, various pyogenic organisms, such as staphylo-, strepto-, pneumococci, influenza bacilli, etc.

The ichorous fluid in gangrenous cavities is alkaline in reaction when fresh, and contains the decomposition products of organic matter along with tissue fragments, blood pigment in all its stages of change, and lung pigment. Most of the connective tissue and elastic fibers of the gangrenous portions are dissolved, but some fibers remain. From the sputum in gangrene of the lung, Filehne prepared a glycerin extracted ferment resembling trypsin, which dissolved elastic fibers in alkaline solution. Larger and smaller ragged fragments in the fluid attract attention as lung tissue remains; innumerable bacteria and large numbers of the leptothrix pulmonalis (Leyden, Jaffe) are also present; fat droplets, and needles of fatty acid, the so-called magarin crystals, are also found. The latter are fine curving needles, often gathered in bundles; they dissolve on warming. Leucin and tyrosin may also be present. Occasionally, moulds are encountered (aspergillus), especially in diabetics in whom the organic constituents are rich in glucose and glycogen.

In addition to the large bacterial flora, three anaerobes, bacillus fusiformis, comma bacilli (spirillum sputigenum), and spirochetae identical with those of the mouth cavity and culturable (comp. Arnheim), are usually found in the gangrenous material, especially in illy-defined foci. They are especially numerous in the borders between necrotic and healthy parts. In forms sharply demarkated, bacteria are less abundant, and cocci predominate (Buday).

Non-putrid gangrene due to aspiration is very rare; such foci of dirty black color and pulpy consistency contain moulds, especially aspergillus (p. 480), or sarcina ventriculi, as causes of the odorless gangrene.

Usually, the parenchyma in the vicinity of a recent abscess or gangrenous focus responds by an active reaction and much fibrin and blood appear, but the decomposition process may spread in such hepatized tissue. Dead parts may be completely detached like a sequestrum.

**Course.**—Pulmonary abscesses and gangrene are usually fatal but in a few cases, the focus is walled off by granulations from the interstitial tissue, the part is encapsulated and finally becomes a contracting scar, less frequently in embolic foci than in aspiration foci, since the former are multiple, as a rule, and appear in septic diseases otherwise fatal.

Another mode of healing is by evacuation into a bronchus, or by surgery; cicatricial healing occasionally occurs, usually only when the focus is small. The cavity is occluded by granulations, its walls grow together and leave a pigmented scar. On the other hand, rupture of a larger confluent abscess into a bronchus seldom leaves a smooth-walled cavity system communicating with the bronchus, but the author saw such a cavity almost as large as a hen's egg in a woman 36 years of age who died in the fifth week of puerperal fever (thrombophlebitic form); at one time the patient expectorated much sputum containing enormous numbers of streptococci, probably from evacuation of an abscess into a bronchus. At the time of autopsy, the communication between the bronchus and the cavity was no larger than a pinhead. In a similar case, the author saw a fibrous trabeculated gangrenous focus the size of a small apple.

Diffuse gangrene of the lung, as usually combined with fetid bronchitis, rarely becomes chronic. The picture is complicated chiefly by secondary interstitial tissue proliferation which leads to partial atrophy of alveoli (cornification), to thickening of the septa, massive pleuritic adhesions and the formation of bronchiectasias. The alveolar parenchyma is friable in early cases, filled with blood and gas bubbles, dark brown or gray and turbid after washing, finely meshed with many irregular cavities with ragged walls; in older cases, the gray, glassy speckled picture of chronic catarrhal pneumonia with its accumulations of yellow fat granules is seen (doubly refracting substances) (see p. 408).

The dangerous complications of purulent and gangrenous foci must be mentioned: pleuritis with purulent or gangrenous pneumothorax; the pleura, perforated by multiple small holes, covers the gangrenous focus with a yellowish or yellowish green, friable, necrotic membrane; pericarditis; rupture of a cavity into a bronchus with subsequent secondary miliary gangrenous foci or diffuse gangrenous bronchopneumonia; hemorrhage from an eroded arterial branch is rare, but may prove fatal (hemoptysis).

**Pathogenesis of Suppuration and Gangrene of the Lungs.**—In abscess-forming and gangrenous bronchopneumonias, the changes are bronchogenous by continuity of a chronic purulent or putrid bronchitis to the parenchyma as multiple foci, often miliary in size, or as diffuse suppuration, or necrosis, or abscess formation and gangrene from infected foreign bodies.

The latter are usually food particles which enter the respiratory tract during belching, vomiting or swallowing, especially in those with defective epiglottis, or in the insane, or in those who are very ill. They are, however, often formed in the body itself by inflammatory or necrotic decomposition, *e.g.*, particles of sloughing carcinomas of the upper tracts, especially the tongue and larynx, aspirated portions of gastric or esophageal carcinomas, bacterial plugs from carious teeth or tonsillar crypts, (see under mouth cavity), fragments of carious teeth, tumor secretions from the mouth, throat or pharynx. Probably the most frequent are fragments of esophageal carcinomas perforating the respiratory tract, or food particles entering the respiratory tract through the perforation. Rupture of a softened anthracotic lymph node into a bronchus (usually the right) and into the esophagus often causes gangrene, especially in advanced age (see Sternberg).

The so-called vagus pneumonia is a deglutition pneumonia; section of the vagus is followed by paralysis of its branch, the recurrent nerve, and the side of the larynx innervated by it, by which entrance of secretions or food is favored. These swallowing or aspiration pneumonias are situated most frequently in the lower and middle lobes; they are very small to lobular bronchopneumonias, occasionally simple catarrhs, but usually suppurations and gangrene of the lung parenchyma.

In the beginning, the foci are grayish red, somewhat granular, the size of linseeds to peas; they soon become purulent or gangrenous and the parenchyma liquefies. As the disease progresses peripherally, diffuse infiltrations occur with more suppuration and gangrene; the tissues are discolored and soft, friable and dry in the beginning, later cavitated by liquefaction, and black masses are expectorated. Old scars, residues of previous pneumonias, etc., predispose to gangrene, according to Schridde. A single foreign body often causes an extensive indurative process (comp. p. 417).

A. Paltauf attributes aspiration into the lower and middle lobe to ordinary or quite superficial breathing (under anesthesia, insane, somnolent people), into the upper lobe to forced or deep breathing. This rule can be applied to death by drowning. The upper lobes expand when there is an impediment to respiration, *e.g.*, in diphtheria or tracheal stenosis. According to Stubenrath, any liquid, if it cause drowning, produces inflammations of the bronchi and lungs, with but one exception—the intrauterine aspiration of sterile, meconium-containing amniotic fluid, when the child breathes too soon. Meconium bodies can be demonstrated microscopically in the lungs.

Abscesses and gangrenous foci (circumscribed gangrene) may be of hematogenous origin (metabolic embolic), by occlusion of larger branches with larger septic emboli, or microscopic particles in the pulmonary capillaries. These processes in septic embolism have been discussed on p. 386. According to the kind of microorganism, there develop abscesses or gangrenous foci or both. The name employed is metastatic or embolic, suppurative, or gangrenous pneumonia, or hematogenous septic focal pneumonia.

The emboli consist of bacteria alone, or of bacteria in pus or gangrenous masses, or of infectious thrombi, especially in puerperal fever, (see Bingold, anaerobic streptococcus as cause of gangrene), but also in otitis, malignant endocarditis of the right heart, osteomyelitis, furunculosis, phlegmon, sometimes in incarcerated hernias, gangrenous appendicitis, dysentery, etc. When a larger branch of the pulmonalis is occluded by a septic embolus, the necrotic infarct is sometimes demarkated from the infected surrounding connective tissue; it then undergoes liquefaction, a pus cavity is formed, and putrefying organisms lead to gangrene. Similarly, when minute branches or capillaries are occluded, the resulting inflammatory foci of gray or grayish red color soon undergo suppuration or gangrene, or the latter occur immediately, without previous inflammation. Sometimes the foci are similar to hemorrhagic infarcts (comp. septic hemorrhagic infarct, p. 385).

Microscopically, the beginning change is cellular infiltration of the walls and vicinity of the occluded vessels, and fibrinopurulent or hemorrhagic exudation into the adjacent alveoli; later disintegration produces the typical abscess or gangrene. Large numbers of bacteria are found in the capillaries, interlobular vessels and within the alveoli; staphylococci and streptococci are the most frequent causes of abscesses.

Small, rounded, firm foci, peripherally located in large numbers, occur without coarse embolism, frequently with suppuration and gangrene. This involves the pleura by continuity or rupture, the latter followed by pneumothorax if a bronchus is opened.

Abscesses and cavities may be crowded so closely together that the whole lung gives forth a cavernous sound.

Other causes of abscesses and gangrenous foci (p. 400) are croupous pneumonias with secondary causes added, such as aspirated foreign substances or a coincident older putrid bronchitis. This is frequent in drinkers. Even a simple catarrhal pneumonia may undergo secondary gangrene.

Trauma, direct and indirect wounds, such as contusions, crushing without external lesion, may initiate the abscesses and gangrene, but if infection from without on clothing, etc., or from within from a bronchus is added to the injured, blood infiltrated lung, gangrene is more likely than abscesses (comp. lit. p. 378).

An infarct, originally simple hemorrhagic, becomes purulent or gangrenous by infection through the respiratory tract. Gangrene-producing microbes secondarily invade the lung (p. 346), from old tuberculous cavities, even if smooth-walled and healed, or from bronchiectasias.

Gangrene is frequent in diabetes mellitus, and also a non-putrid necrosis (pneumomalacia) with perhaps extensive destruction. The lung, pale in color and friable, contains cavities, similar to those in pneumomalacia acida (comp. p. 358; see there for differential diagnosis).

"Septic pneumonia of the newborn" is a designation given to the abscess-forming pneumonias caused by infection via the respiratory tract. The alveoli contain large numbers of microorganisms. Sometimes the mothers are septic at parturition, so that there is a possibility of intrapartum transmission. Other septic infections of the newborn by way of the umbilicus may extend directly through the lymphatics and cause purulent peritonitis, pleuritis, pneumonia (really peripneumonia), or indirectly via umbilical thrombophlebitis and pylophlebitis (see under liver), to produce embolic pneumonia.

**Translator's Remarks.**– For postoperative lung abscesses and gangrene, aspiration or embolism from the wound, clinical and treatment, see Meyer, W., Arch. of Surg. 6: 361: 1923. Cutler, E. C. and Schlueter, S. A., Ann. Surg. 84: 256: 1926. Holman, E., Chandler, L. R. and Cooley, C. L., Surg. Gyn. & Obst. 44328: 1927. For spirochaetal pulmonary gangrene, see Maes, W., Internat. Clinics Vol. 2, series 36, 1926, Lippincott.

**Acute Interstitial Pneumonia.**— Interstitial pneumonia is very characteristic in cattle; the lymph vessels are as large as goose quills, varicose, and filled with a yellow substance; when older, they are surrounded by cicatricial tissue and course through the hepatized lung like the veins in marble.

Such inflammations are usually suppurative, and localized in the interlobular, and intraalveolar interstitial tissue and sometimes in the peribronchial regions. Most frequently they are conducted from an inflamed pleura in such close relationship to the course of lymph vessels that the process has been called "interstitial lymphangitic pneumonia," or "peripneumonia." Originally a pure interstitial affection, *i.e.*, essentially a pulmonary lymphangitis, it frequently extends to the surrounding alveoli which are filled with cellular, serous or cellular-fibrous, sometimes bloody exudate, to the exclusion of air. This usual type extending from the pleura to the lungs is also called pleurogenous pneumonia, and in this the most characteristic macroscopic changes can be seen.

The suppurative, or suppurative fibrinous pneumonia which is the starting point, may be of various origins, such as subsequent to a pulmonary abscess, or metastatic in pyemia (especially puerperal), or secondary to peritonitis or to trauma (infected wounds of the pleura).

On removal of the exudate, the pleural surface is found etched with broad yellowish white connected strands following the lobular boundary lines; these are infiltrated lymph vessels filled with pus, or fibrino-pus. On incision, their contents can be squeezed out. Section through the lung reveals broad pus channels following the connective tissue septa which are occasionally as thick as a lead pencil, varicose and rounded, almost abscesses. In influenza pneumonia, areas are sharply demarkated, but their peripheral portions are soon infiltrated by extension of the perilymphangitis. The bronchial walls are also infiltrated and the mucosa is covered with purulent exudate; indeed, the interstitial tissue may actually disintegrate, so that many fields seem like sequestrated necrotic plugs (pneumonia dissecans).

**Results.**—If death does not terminate the process, the connective tissue is always thickened, progressively so, if the inflammation acquires a chronic productive character (comp. under chronic interstitial pneumonia).

But pleurogenous pneumonia is not the only form of acute interstitial lymphangitic pneumonia. Peribronchial lymphangitis has already been discussed; it results from the peribronchitis of acute bronchitis (p. 347) and the alveolar parenchyma is secondarily involved (peribronchial pneumonia).

Primary pneumonia dissecans is a rare and serious disease, probably bronchogenous in origin, developing sometimes in septic processes and sometimes in influenza (comp. under influenza, pp. 341, 390, 387 and 403).

Inflammations may also enter through the lymphatics from the hilum of the lung, vertebral caries, suppuration of mediastinal lymph nodes, etc.

As Buhl emphasized, suppurative peribronchial lymphangitis is an important complication in phthisis, for when it extends to the adjacent parenchyma, it helps to hasten disintegration.

**Chronic Interstitial (Productive, Fibroplastic) Pneumonia. Contracted Lung.**—This is a chronic plastic inflammation of the connective tissue scaffolding of the lung producing granulation tissue which changes to firm connective tissue. The lung is hardened and indurated, its septa are thickened, it shrinks to greater or less degree; since it is often accompanied by anthracotic pigmentation, the process is called slaty induration.

*Cirrhosis.*—(For original meaning of the word, see under cirrhosis of liver.)

Several forms are differentiated, according to the location of the productive inflammations, *i.e.*, in the larger septa (*a*), in interlobular, peribronchial and perivascular connective tissues, or in finer septa (*b*), inter-

Fig. 188.—Chronic interstitial pleurogenic pneumonia in conjunction with chronic pleuritis; piece of lower lobe; nat. size.

alveolar or peribronchial. In extensive cases of the first type (*a*), the lung is marked like a checkerboard with sinewy white, or black pigmented, coarse strands of connective tissue; it is seen best when a pleurogenous lymphangitic pneumonia becomes chronic and fibrous (fig. 188).

In the second type (*b*), the loose parenchyma is transformed to a vascular, tough, fleshy, airless, tissue (cornification or induration), by invasion of the alveoli with connective tissue, as discussed under chronic croupous pneumonia (p. 398), or by compression of the alveoli which produces the gland-like appearances mentioned on p. 399 in the thickened contracting septa (contracted lung cirrhosis).

The changes involve one or more entire lobes or parts. In the first instance, the lung is hard, and shrunken, its surface is attached to the

costal pleura and to the diaphragm, making its removal impossible during autopsy, without actually excising it from the cicatrized mass. Portions which escape contraction are emphysematous. The color of the indurated tissue varies from white, grayish red to dark blue gray or slaty when rich in coal pigment (fig. 197). The bronchi are distended, the purulent bronchitis is present. The pulmonary artery of the cirrhosed lobe is sclerotic (comp. Evans).

As a rule, however, induration is confined to local areas, especially the apices, in which occasional inclusions of true bone are found.

The causes of productive interstitial pneumonia are quite varied. It is often a curative reparatory process, as in the cicatricial healing of an infarct, encapsulation of abscesses, gangrenous or caseous foci, in the healing of other ulcerative cavities such as bronchiectasias or phthisical cavities, etc.; it is also a reparatory process in the healing of wounds. Superficial tears from fracture of ribs, stab and bullet wounds may heal in a few weeks and leave a scarcely visible scar. The blood in the vicinity is penetrated by granulation tissue. This healing may take place without fever, which seems to show that the normal lungs and finer bronchi are practically sterile (A. Schmidt). Perforating bullet holes, under favorable conditions, heal to linear completeness, but even when the process is disturbed and suppuration and gangrene are added, smooth-walled fibrous-lined canals may be the end results. Sometimes projectiles are encapsulated within the lung (see Merkel, war injuries of the lung, also Konjelzny, prognosis of bullet wounds of lungs, aneurysm of the pulmonary artery, productive hemorrhagic pleuritis, secondary hemorrhages, etc.).

In other cases, productive interstitial pneumonia joins older lesions in the alveolar parenchyma, or croupous pneumonia with collapse when it is followed by induration.

Foreign bodies also stimulate extensive indurative processes, *e.g.*, an aspirated bone fragment, or, as the author saw, the mouthpiece of a cigar holder in the lower main bronchus. Cicatricial adhesions are often especially dense on the diaphragm.

It may follow an acute suppurative lymphangitic interstitial pneumonia which is so often a pleurogenous affection (fig. 188), but other less severe inflammatory changes in the pleura may also extend to the septa, especially through pleural adhesions as at the apices in which interstitial pneumonia is practically always present. Thus, the peripheral septa are thickened, but the connective tissue formation is often marked enough to give an extensive pulmonary cirrhosis, which, emphatically said, can occur independently of tuberculosis. Productive interstitial pneumonia is extraordinarily frequent in dust inhalation.

v. Hansemann described a chronic reticular lymphangitis leading to the formation of a fine gray network as an independent disease of unknown etiology.

See chapter VII in reference to the chronic interstitial changes in infectious granulomas (tuberculosis, syphilis, actinomycosis).

**Diseases Caused by Inhalation of Dust. Pneumoconioses.**—Inspired air contains many kinds of dust which act essentially as mechanical irritants. Small quantities are borne without harm, but habitual inhalation of large amounts is always followed by chronic changes in the lungs, depending to a certain extent on the kind of dust.

Toxic, caustic, and infectious dusts, which Heim and Agasse-Lafont differentiate as active, in contradistinction to the passive kinds which cause the well known chronic pneumoconioses, cause acute and progressive diseases, chiefly pneumonias (comp. Thomas's, phosphate flour pneumonia, p. 407). It is not correct to speak of these conditions as pneumoconioses.

While everyone inhales small quantities of carbon, certain occupations are more "dusty," not only from coal particles, but also from much more irritating things such as stone, metal and organic dusts.

**The Fate of Inhaled Dust and the Changes It Causes in the Lungs.** A large quantity of dust is stopped in the nasal and pharyngeal mucosa. Some reaches the bronchi and is found free or in cells (wandering and epithelium), and may be carried out by the activity of cilia or by expectoration. Continuous inspiration of irritating dust over a long time, or larger quantities of otherwise harmless dust cause catarrh of the bronchial mucosa, and the appearance of many dust cells, free, and in the inflamed bronchial walls. A fraction reaches the alveoli and remains free, or in cells which are gradually loaded with the particles. According to Haythorn, pigment phagocytosis is done chiefly by endothelial wandering cells derived from connective tissue (comp. p. 9).

The irritation is apt to cause a slight alveolar inflammation expressed as a serous exudation, desquamation and proliferation of the epithelium, *i.e.*, a desquamative catarrh. With loss of the epithelium, collapse induration occurs. These small inflammatory foci may sometimes be designated as miliary bronchopneumonias.

Most of the dust in the alveoli is transported by the lymph channels into the interstitial tissue and bronchial lymph nodes as free pigment or in lymph cells. It takes its course through the "stomata" (minute gaps in the epithelial lining of the alveoli), or through the cement lines between the epithelium into the perialveolar tissue spaces, then into the larger lymph tracts and to the peribronchial lymph nodules provided these channels are not closed by previous pathological processes. Otherwise, it is arrested, but quickly reaches the bronchial nodes which retain most of

it. In animals, this transport occurs in a very short time, even a few hours. It may finally reach the cervical, mediastinal and epigastric lymph nodes.

On the basis of experimental work, Calmette and his pupils, Vansteenberghe and Grysez, claim that soot in the stomach and intestines reaches the thoracic duct through the lymph and enters the blood and lungs in this way, having thus the same enterohematogenous route as pulmonary tuberculosis. Many investigations tend to disprove this conception (see lit. by Beitzke and in appendix). Later, Arbeiter supported it; at the present time it must still be considered true that the main mass of dust reaches the lung by inhalation.

Pointed, or sharp splintered dust may bore directly into the alveolar walls and reach the interstitial tissue, as demonstrated experimentally by Arnold (comp. Lubenau). During its passage through the tissue lymph channels, the particles may injure the tracts themselves, and start inflammatory proliferations in and around the lymphatics followed by induration of more or less extent. The lymph vessels undergo atrophy, and the pigment remains free, or in cells in the interstitial tissue. Some forms of dust, especially stone dust, vigorously stimulate productive inflammation with the result of nodular or beaded fibrous thickenings which are called dust nodules, dust scars; severe degrees may produce actual cirrhosis (see p. 416).

This indurating fibroblastic inflammation extends to the pleura; the surfaces adhere and are thickened to a massive shell. Bronchiectasias are frequent in cirrhotic lungs, due not only to the retraction of scar tissue, but also to the chronic bronchitis (fig. 197).

When the bronchiectasias suppurate and ulcerate, the cavities may continue into the adjacent parenchyma as so-called chronic abscesses, a term not always correct since, if they are old, the cavities contain not pus, but viscid mucus. The wall consists of the mucosa of the bronchiectasia, or since it ceases to be an independent structure, the cavity is surrounded by indurated lung tissue filled with coal or stone dust, see p. 420 (black phthisis, easily mistaken for tuberculous cavities!). But it must be remembered that bronchiectasias may become tuberculous and that true tuberculous ulcers may be secondary.

**Pneumoconioses in Relation to Tuberculosis.**—The injury to lymphatics and the catarrhal condition of the respiratory tract in many pneumoconioses favor infection, which is perhaps further aided by the fibrous thickenings which impede respiratory activity (comp. Tendeloo) and prevent the absorption of pneumonic exudates. They are predisposing causes of tuberculosis. The high percentage of phthisics in occupations associated with the inhalation of dust is remarkable, especially so among stone cutters, and metal grinders (comp. Berglund); lime dust, on

the other hand, is supposed to be protective and curative, (comp. Villaret, E. J. Neisser, and references by Beitzke).

It has been observed that the course of tuberculosis is frequently mild in marked anthracosis and shows a tendency to heal (comp. Cesa-Bianchi). As stated by Klotz and Haythorn, the progress of the tuberculosis is inhibited by pigment, occlusion of lymph channels, or atrophic occlusion due to fibrosis stimulated by anthracosis; secondly, the fibrosis perhaps helps encapsulate tuberculous foci.

In reference to the rumored relation between anthracochalicosis of the lungs and the bronchial nodes to broncho-pulmonary carcinoma, see under carcinoma.

**Different Forms of Pneumoconiosis.**—Pulmonary anthracosis. Coal pigment lung.

The most common dust which enters the lungs is carbon as the very small soft harmless particles of soot from smoke, or as dust of hard unburned coal, in larger, irregular, pointed angular irritating particles.

The lung in the newborn contains no pigment, but spotting from coal pigment often begins in the first months (Lubarsch), or according to Shingu, from the twenty-third day. The black spots on the surface are often arranged corresponding to the borders of the lobules. Sometimes the parts corresponding to the intercostal spaces show more pigment than those lying against the ribs which show spotted, parallel black striae perhaps on both visceral and parietal pleurae (Klotz). Others declare that the costal striae are the more pigmented (Beitzke). The spots frequently become small black nodules (p. 340) from addition of indurated connective tissue. As on the surface, so in the interior of the lungs, the lymph channels and follicles (p. 340) decide the localization of the coal. Black nodules are present in the peribronchial connective tissue, and in the periphery of the lobules, while striae and spots occupy situations between. The pigment is always abundant in the arterial wall lymphatics and may even reach the intima. Moderate quantities cause no injury.

Larger quantities, as inhaled by chimney sweeps, stokers, charcoal burners, coal mine workers, etc., cause bronchial catarrhs, anthracite desquamative alveolar catarrhs (bronchopneumonia), and interstitial pneumonias. Portions of the lung become airless, hard and black. Nodular foci contain coal particles and coal deposits surrounded by concentric masses of connective tissue. In other cases, diffuse, fibrous, pigmented, firm or sometimes turf-like friable thickenings involve large portions of parenchyma (slaty or anthracotic induration).

Softening of the black foci may occur with cavity formation usually of irregular or globular shape, surrounded by black, friable or poultaceous masses somewhat resembling India ink. This is called "black phthisis"

(phthisis atra). The focus may open into a bronchus, and is easily mistaken for ulcerative tuberculosis.

Deposits of soot are favored by changes already existing, such as fibrosis of the interstitial tissue chiefly due to stone dust. The essential factor is the destruction of the transportation channels, *i.e.*, lymphatics, and, naturally, all other indurating inflammations in the pulmonary connective tissue favor the deposit for the same reason. Blocking of the lymphatics by pigment and fibrosis makes the absorption of exudates more difficult.

The bronchial nodes are black, usually hard, but occasionally soft from periadenitis, when they may rupture into blood vessels (pulmonary arteries and veins, branches of the cava, azygos), bronchi or trachea. Pigment masses emptied into veins may reach the spleen, kidneys, liver, etc., (Weichert). But even without rupture, in severe anthracosis, coal pigment can be found in these organs, presumably transported through the blood after direct entrance from the lungs (Soyka). Anthracosis of abdominal lymph nodes is probably due chiefly to retrograde transport, but others believe in transport by way of the efferent canaliculi of the mucosa, or by the blood stream (comp. Beitzke and his discussion). Comp. in reference to bronchial lymph nodes p. 254; pigment embolism under lung, p. 388; and under esophagus, traction diverticuli.

**Differentiation between Coal Pigment and Black Blood Pigment.**—The lung may contain granular black pigment derived from hemorrhage. This is the iron-containing decomposition product of hemoglobin, the black (melanotic) granular hemosiderin which is very resistant to reagents. (The other decomposition product of blood is the iron-free, usually crystalline, rarely granular, hematoidin.) Coal and hemosiderin can be differentiated, because the latter is quickly destroyed if treated with chlorine and diluted liquor potassae. Black blood pigment is dissolved by sulphuric acid when its red color reappears, (iron reaction, p. 372).

**Chalicosis Pulmonum. (Stone Cutters Lung.)**—This is due to the inhalation of stone dust, and frequently has reference to silicates which may be found in the lungs as sandstone, quartz, flint, quartz sand and quartz crystals. It is the most dangerous dust, for it bores into the lung tissue and cannot be removed. It causes nodular, cicatricial interstitial pneumonias and stony hard pleural nodules (histology by Arai). The nodules are usually very small and consist of concentric layers of connective tissue which enclose the dust, but if much is present, the lungs are filled with nodules and nodes of various colors from grayish black, or if much coal is also retained, to deep black within which arteries and bronchi break down. They are so hard at times that they cannot be cut. The dust may contain up to 24% and more of silicic acid (Kussmaul-Schmidt).

The other portions of the lung may be emphysematous, and bronchiectatic; cavities are very frequent. The pleura may be thickly covered by grayish white, cicatricial, stone dust-containing dots and nodules with frequent massive thickenings. But not all of the dust remains permanently in the lung, for some reaches the bronchial nodes. Calcium carbonate is dissolved by the body juices (v. Ins). In some occupations, such as grinding, stone cutting, file cutting, both stone and iron dust are inhaled (comp. Staub-Oetiker). For stone cutter's lung and tuberculosis, see p. 419.

**Pulmonary Siderosis.**—The inhalation of iron dust generally produces severe pneumoconioses (first observed by Zenker). The lung is black red or black, according to the relative amount of red iron oxide inhaled, *e.g.*, the red polishing powder for steel or mirrors, the iron-containing red sand stone, or ferrous oxide or phosphate in the manufacture of paper. Diffuse red or black indurations develop with less nodule formation than in chalicosis.

**Other Forms of Dust.**—Deposits of clay (aluminosis, generally aluminum silicate) produce a grayish green color observed in workers in porcelain or ultramarine factories. The dust of tobacco (in workers with tobacco) produces a dirty brown color. Organic dusts such as tobacco, hair, cotton, wood, are violent irritants of the respiratory tract and very hard to remove from the lungs (lit. by Sticker).

### Infectious Granulomas of the Lungs

**Pulmonary Tuberculosis.**—The changes under discussion are the effects caused by the bacillus tuberculosis discovered by R. Koch (1881) and cultivated, experimentally demonstrated, and found histologically by P. Baumgarten.

According to R. Koch, who again expressed his opinion at the International Congress for Tuberculosis in Washington in 1908, which has never been disproved, pulmonary tuberculosis in man is always caused by the tubercle bacillus of man and never by the tubercle bacillus of cattle (comp. in reference to this, p. 489). (See lit., No. 1908, 47 and p. 489.)

The organism is a delicate rod with rounded ends, about four microns long, often curved or kinked, non-motile. Lighter gaps in the rod are frequent and considered by some to be spores (Koch, Betegh), by others to be vacuoles (Weichselbaum); they give a granular appearance to the organism. The granular form can be demonstrated by the modification of Gram's stain given by Much, but not with Ziehl's method (not acid fast, but antiformin fast). See lit. by Lichtenhahn, Barnowsky, Bittrolff, Momose, Bruckner, Werner, Much and p. 271.

(In reference to ray fungus forms of tubercle bacillus in the animal body, comp. p. 466.) Culture: they can be grown on blood serum or glycerin agar. Apart from cultures, they do not grow outside the body. They stain with difficulty, but if, as usual, they have been treated with penetrating dyes (aniline colors such as fuchsin or gentian violet, the watery solution of which has been fortified by alkali, aniline or phenol), they retain the color tenaciously, and do not decolorize even when treated for a short time with acid (25% hydrochloric, nitric, or sulphuric acids). All other organisms are soon decolorized in acid with the exception of the acid fast bacilli of smegma, leprosy, of tuberculosis of fowls, and some others such as the butter bacillus of Rabinowitsch, Moller's bacillus of timothy, grass and cowpen manure. With this in mind, the term "specific staining" of the tubercle bacillus may be used. If, after red or blue staining and acid decolorizing, a counter stain such as aqueous methylene blue or Bismark brown is used, other bacteria and tissue particles are stained. To observe the latter, it is advisable to counterstain with hematoxylin after using the "specific" stain of Ziehl Neelsen (carbol fuchsin).

The condition of being acid fast and the consequent color reaction depends on their fat content (Klebs, Koch and others) or chitin content (Helbing) or on their physical peculiarity (Philibert, v. Betegh, lit.). [For the parasitology of the tubercle bacillus, see White W. C., Arch Path. & Lab. Med. 3; 84; 1927.—*Translator.*]

To understand the pulmonary changes, sometimes very complicated, requires some general preliminary observations.

First, the effect which the organism produces by penetrating lung tissue must be considered. To Baumgarten is due much credit for our knowledge of these processes. The histogenesis of the miliary tubercle, in short, the formation of "the tubercle," is this: the organism enters, multiplies and injures the tissue, but stimulates fixed cells of connective tissue and epithelial origin into a proliferation (mitosis); this may be called a productive inflammation. Milium, millet-seed, as designations of size must not be taken too literally; more frequently the tubercles are "submiliary." According to Wechsberg and Herxheimer, the first effect on tissue cells and elastic fibers is degenerative, but is followed by reactive inflammatory cellular proliferations. In this way, as a rule, but not unqualified (Schmaus, Justi), a non-vascular, translucent, gray nodule the size of a millet seed or pin head appears, composed of relatively large epithelioid cells. Even if the bacilli reach places where there is no epithelium, epithelioid cells (fibroblasts) may develop by proliferation of fixed connective tissue cells. Many are large giant cells with many nuclei arranged peripherally. According to one opinion, these giant cells develop by fusion of numerous single cells, or of endothelial lined hollow spaces such as capillaries, lymph

vessels (confluence theory), while according to the proliferation theory of Baumgarten, they result from continued nuclear division without subsequent cytoplasmic division; the greater part of the cellular content dies, (Weigert, later opinions by Wakabayashi, who never saw necrosis in the cell body; Herxheimer-Roth, Robbers, lit.). The less the tubercles grow, and the less bacilli present, the quicker the formation of epithelioid and giant cells.

Between the cells of the tubercle are delicate fibers, the so-called tubercle reticulum, visible only in thin sections. These are partly remains of the split and dissolved fibrillar bundles of local connective tissue, and partly prolongations of the cells of the tubercle; perhaps some are newly formed fibres. In addition, round cells are found in the nodules; they appear in great numbers (according to Sternberg, less if the tubercles are young) from the surroundings and come to rest at the periphery of the tubercle, and (often in great abundance) between the epithelioid cells. They are mostly lymphocytes, with a few plasma cells, and isolated polymorphonuclear leucocytes added. (Concerning the bactericidal power of the lymphocyte, and its power, probably by means of a lipase, to destroy the acid fastness, general virulence and the caseating components of the bacilli, see Lichtenstein, lit.) Fibrin derived from the blood vessels of the vicinity may also appear around and within the tubercle. It is assumed that the toxic products of the bacillary metabolism which saturate the surroundings, exert an inflammatory, irritative effect on the vessels, leading to exudation and cell migration; the stimulus is greater, the greater the number and multiplication of the organisms. (See v. Baumgarten in opposition to Heiberg, who considers collections of large mononuclear round cells—such as macrophages and polyblasts which are surrounded by plasma cells and small round cells—as precursors of the typical epithelioid tubercle.) The focus sooner or later disintegrates, becomes necrotic and caseous usually beginning in the center. The caseous substance is a finely granular or striated, somewhat hyalin mass without cellular structure and nuclear staining power.

It must be emphasized that not every tubercle necessarily has the structure just described; there are miliary tubercles of almost pure lymphoid composition—lymphoid or small cell tubercles—in which the lymphocytes greatly outnumber the other cells, as in meningeal tuberculosis. On the other hand, caseation sometimes develops so quickly that neither giant cells nor epithelioid cells can be seen (see case, p. 429).

Bacilli are found here and there, singly and free between the cells of the tubercle, but more usually in the larger epithelioid and giant cells. Curiously enough, in typically formed epithelioid tubercles they are apt to be scarce. The bacteria disappear in time in the caseous areas, but

often can be stained in their periphery although they have been found in masses in the center of caseous debris. The same statements are true of larger conglomerate caseous foci. In caseating giant cells, the bacilli are usually situated in the periphery where nuclear staining points to retained life. While in many cases the tubercles become completely caseous under the constant necrotizing influence which injures newly formed cells and also prevents the formation of connective tissue and new vessels, in other cases, especially the chronic forms, this influence dies out, and a fibrous metamorphosis of the tubercle occurs, chiefly in the non-caseated margins (caseous-fibrous tubercle). Thus a sort of capsule is developed around the caseous interior, or indeed, the fibrous tissue invades the whole nodule even without central caseation (so-called fibrous tubercle). The latter result is a perfect cure. During this process perhaps the cells themselves of the tubercle change into connective tissue. A hyalin metamorphosis is not less frequent, and involves not only the fibres of the reticulum but also some of the cells and those parts of the tubercle which show fibrous changes.

**Translator's Remarks.**—For the mononuclear phagocytes of the lung with reference to tuberculosis and other conditions, see Permar H. H., Am. Rev. of Tuberculosis 9, 507: 1924. For discussion and data on the anatomical structure of tubercle from histogenesis to cavity, see Krause A. K., Proceeding 5th Conf. of Internat. Union against T. B. pub. Nat. T. B. Assoc. of U. S. New York City, page 161.

## EFFECT OF TUBERCLE BACILLI AND THEIR TOXIC PRODUCTS OF METABOLISM ON THE LUNGS

**Relation between the Formation of Tubercles and Tuberculous Pneumonia.**—It will be seen that invasion of the lung by the tubercle bacillus causes two different changes which apparently are not related at all: (1) the formation of tubercles, *i.e.*, cellular structures, from tissue inflammatory products in the form of nodules, and (2) the appearance of productive exudative, or particularly exudative pneumonic, processes which may be called either caseous or gelatinous lobular pneumonias. All productive changes tend to caseation necrosis of tissue; while in the gelatinous form of tuberculous pneumonia, this is not always necessary, in fact, absorption is still possible. Tuberculosis and caseous pneumonia are but different forms of the same infectious disease; in reference to their anatomic relations, several opinions are expressed, which will be touched upon later. Only it must be remembered, as we have seen in the histogenesis of the

tubercle, that the bacillus and its toxins may exert either a productive or an exudative inflammatory stimulus, or both at the same time. That the toxic metabolic products alone can produce a most active exudative inflammation is shown by the use of the tuberculin of R. Koch. This yellowish brown fluid prepared from pure cultures of the bacilli contains only the toxins elaborated and no organisms. Subcutaneous injection causes fever and active reaction in areas which contain tuberculous changes; if they are freely visible, *e.g.*, in skin lupus, the effect can be directly observed as consisting of tremendous hyperemia and marked exudation.

Sometimes productive changes predominate, at other times exudative changes are the chief effects. Baumgarten, A. Frankel and Troje assume that the organisms themselves cause chiefly the former, while their metabolic products induce the latter. The opinions of these authors are extremely valuable in understanding the complicated processes in tuberculous lungs, although they are not verified in every point, but are supported and supplemented by the latest researches. They may be presented briefly in this way:

Proliferative processes predominate in the presence of the organisms which give off but little toxin into their surroundings. Then there is principally tubercle formation from connective tissue cells and alveolar epithelium, but opinions are divided as to the relative quantitative participation. According to the animal experiments of Kockel and others, dead bacilli cause practically the same reactions at first as the living organisms, probably on account of adherent toxins. Non-virulent bacilli, *i.e.*, those which have lost their virulence in an immunized organism, act like foreign bodies. As a rule, the local nodules do not become caseous because the presence of the organism is necessary to produce necrosis; it must also have retained certain properties to produce caseation, (p. 424); indeed, the nodules are fibrosed during healing and the process ceases. But, on the other hand, caseation does sometimes occur after moderate injections of tubercle bacilli killed by heat (see Roger and Simon, Lichtenstein). The action of a chloroform extract is similar to that of dead organisms (Jaffe, lit.). The hypothesis of Lichtenstein states that those organisms which have been deprived of fat by lymphocytic lipase, and are thus not acid fast, lose their caseating power, but have a tendency to stimulate fibrous change in the form of a granulation tissue of the character of lymphogranuloma (see p. 270).

Wherever organisms are present which liberate considerable toxins, there are proliferative processes in the form of epithelioid or true epithelial (intra-alveolar) tubercles, or simple epithelial cell proliferation in the alveoli, without the formation of nodules, plus the exudative processes. Thus tubercles and a tuberculous pneumonia leading to caseation are the

result. The exudate is distinguished by its large amount of epithelium. (Comp. tuberculous pneumonia, p. 437.)

In a situation in which there are no organisms (or not necessarily so), but in which their toxins are present in large quantities ("P distance action," A. Frankel, Troje), *i.e.*, arrive from a distant bacillary focus, an inflammatory exudative change predominates (parallel to the action of Koch's tuberculin). If a large portion of the lung is flooded with this toxin, a so-called smooth pneumonia results (Virchow), called by Laennec, gelatinous infiltration, by Buhl desquamative pneumonia. Baumgarten produced these changes experimentally in rabbits by injecting large quantities of bacilli suspended in fluid into the trachea (see details under tuberculous pneumonia, p. 437).

If, in tuberculous pulmonary processes the result of a uniform etiology, we meet changes chiefly of inflammatory productive nature of which the miliary tubercle may be considered typical, and, in other cases the inflammatory exudative characteristics predominate, as typified by the fibrinous, later caseating tuberculous pneumonia, then it seems less difficult to accept the morphologic dualistic conception. This is especially emphasized by Orth, who believes in a sharp anatomic separation between proliferation with its product, the tubercle, and exudation with its product, caseous pneumonia. But just here a debatable point is reached, since v. Baumgarten, A. Frankel, and Troje are of the opinion that both changes are combined, as a rule, *i.e.*, proliferation and exudation, and that, since caseating tuberculosis is not free of exudative processes, the process of caseation in caseous pneumonia must always include epithelial proliferation. Orth, in opposing this "monistic" conception, lays especial stress on the abundance of fibrin in tuberculous lobular pneumonia in differentiating this from tubercles, and although A. Frankel and Troje, Falk and others have demonstrated fibrin within tubercles, Orth considers these findings of little importance, since they are not constant and the amount of fibrin is but slight. After all, it is wise to remember that every tuberculous process is an inflammation in which it is indifferent whether exudation, proliferation or necrosis predominates (comp. Tendeloo).

Mixed infection, however, must be taken into careful consideration. This means the combined action of the tubercle bacillus with other, especially pyogenic organisms, such as streptococci, the micrococcus tetragenous (which is very pathogenic to white mice, shows capsule formation in the body and in cultures; Boutron calls it micrococcus tetragenous septicus; otherwise it is usually a half saphrophyte, but occasionally causes sepsis—see Ludke—and becomes a true cause of mixed infection), pneumococci, pneumobacilli, etc. This combination is important for the development and particularly for the rapid course of the ulcerative process

in lung tuberculosis. Koch, among others, has pointed this out. But probably it is not absolutely necessary to have mixed infection for the development of ulcerative phthisis as some assume (Babes, Cornet, Marfan, Ortner, etc.). It is also unnecessary to assume that fever is necessarily due to mixed infection, or that mixed infection alone is responsible for the fever, a conception supported by Sata. Indeed, fever may be caused by the action of the tubercle bacillus and its toxins (see action of tuberculin, acute miliary tuberculosis), but is, of course, frequently due to mixed infection also (comp. Kerschensteine, see pp. 440, 456).

Tuberculosis in the lung may be divided according to its locality into interstitial and alveolar processes. The hematogenous miliary tubercle is considered the prototype of interstitial tubercle formation. Doubtless in the beginning it is purely interstitial, partly productive, and partly exudative, but it soon involves the adjacent alveoli. This alveolar process consists, on the one hand, of epithelial proliferation and sometimes the formation of distinct nodules, and, on the other hand, of an exudation (probably chiefly so) usually characterized by an abundance of fibrin.

**How Do Tubercle Bacilli Reach the Lungs?**—They may reach the lungs in three ways: through the blood stream, the lymphatics, and respiration, or by hematogenous, lymphogenous and aerogenous routes.

1. As a rule, entrance of organisms into the blood circulation causes the sudden appearance of nodules of miliary size in the interstitial tissue. They may be isolated, or appear at once in large numbers; the latter case constitutes acute miliary tuberculosis.

2. The organisms reach the lungs by way of the lymphatics from a carious vertebra or rib, or, far more frequently, from a caseous bronchial lymph node after rupture of the capsule and retrograde dissemination (partial disseminating tuberculosis).

3. Probably in most cases the organisms reach the lungs by the air route, after a chronic initial tuberculosis (comp. p. 435).

If we view a given infection of the lung as primary, it was due to the inhalation of organisms with the inspired air, or to aspiration in fluids from the mouth or pharynx into the depths of the bronchial tree, but, of course, the lung may be secondarily infected from tuberculous processes in the air channels.

There must also be mentioned the escape of tuberculous material from a caseous bronchial lymph node into the bronchial tree (main trunk or its branches). This leads to the formation of small (miliary) pneumonic, or so-called peribronchial foci, or severe caseous bronchitis, or extensive caseous pneumonia. It is seen in children (according to Harbitz, quite frequently), and also in adults. According to Ghon, there is always a primary pulmonary focus in such cases.

In various animal experiments, the peculiar sensitivity of the lung to tuberculous infection has been demonstrated. They can be infected by the air route by using but few organisms (Findel and Reichenbach); a much larger number is necessary to infect the intestines; moreover, the organisms injected anywhere will localize especially, and often exclusively, in the lungs (see p. 433).

### Hematogenous (Acute) Miliary Tuberculosis of the Lung

If the term acute miliary tuberculosis of the lungs is used, it signifies that these organs participate in a general miliary tuberculosis, *i.e.*, in a sudden mass distribution of organisms by the blood route to all parts of the body (not one is spared), but always most in the lungs (see above).

There are cases of so-called fulminating tuberculous sepsis (typhobacillosis, Landouzy) in which most minute, quickly necrotizing tubercles are found microscopically in all the organs; these are the severest cases of general miliary tuberculosis. The grave symptoms are caused as always, not by the nodules themselves, but by the dissemination of the organisms and their toxins (comp. Scholz). The author performed an autopsy on a woman 30 years old (tuberculous caries of the 9th thoracic vertebra), in whom, after an illness of 7 to 8 weeks, innumerable small nodules were visible in almost every organ, none of which showed the typical microscopic picture of tuberculosis. Almost all were caseous without giant cells and with few or no epithelioid and lymphoid cells. Toxin action with marked and quick necrotizing effect must have been the cause.

Such general dissemination is brought about: (1) by the entrance of large numbers of bacilli directly into the blood stream (Weigert); either (*a*) by erosive invasion of a caseous focus into a larger vein, or, in the rarest cases, into the cardiac cavity or aorta (Bauer, lit.), or (*b*) by disintegration of caseous nodules, single or multiple, which developed in the intima of a vessel, usually a vein, but also rarely in the intima of the aorta, or the endocardium.

This direct entrance into the blood generally takes place in the tuberculous lung itself by (*a*) erosions of pulmonary veins from a caseous extravascular lung focus or caseous lymph nodes, or (*b*) more frequently in a caseous endophlebitis (tuberculous endangitis, Benda). In the latter, disintegrating multiple (rarely innumerable) caseous tubercles of the intima of pulmonary veins have no relation to caseous foci lying without, but develop as metastases.

Such gross erosions of large veins as mentioned in two observations of the author, p. 159, occur but rarely. Usually it requires long search, often within the lung, to discover even one erosion or a single tubercle of

the intima sufficiently large to explain the presupposed mass introduction of bacilli into the blood. In 123 cases of acute general miliary tuberculosis, Schmorl found 117 in whom vascular foci were found, *i.e.*, 95%; 50 involved the thoracic duct, 39 the pulmonary veins, 3 the right heart, 9 the aorta (7 cases) and pulmonary artery, and 16 others, veins.

In some cases, the general miliary tuberculosis is caused (2) by the organism reaching the blood indirectly by way of the thoracic duct (cf. p. 175).

Indirect invasion occurs from a tuberculous focus, (*a*) when a caseous lymph node ruptures by erosion into lymph vessels which enter the thoracic duct, or (*b*), more frequently from a disintegrating tubercle in the intima of the duct (Ponfick). The bacilli are thus carried into the left subclavian vein, (Weigert). According to Fischer, large numbers of bacteria may enter the lymph (and the blood) from intestinal tuberculous ulcers. Of course, an acute general miliary tuberculosis can develop only when large masses of bacteria and toxins are thrown at once, or in quick succession into the circulation.

Another origin of general miliary tuberculosis, as pointed out first by Koch, from erosion of the smallest vessels in a caseous lymph node, is to all appearances, very rare.

The entrance of toxic products into the blood causes the inflammatory hyperemia and sometimes edema of the lungs. Clinically, it produces fever, and also, perhaps in part, the severe nervous symptoms. The disease proves quickly fatal (weeks).

An acute alveolar emphysema (in children, often interstitial) with the formation of large bubbles is rare. (Emphysema of the skin, on p. 370, see J. D. Wicht.)

General miliary tuberculosis may develop at any age, even the most advanced (comp. Braun). The author saw the condition in an 87 year old woman with caseous masses of mesenteric lymph nodes, also in an 86 year old woman, and in quick succession in two other cases in women over 70 years of age; in the last two there was an old pulmonary phthisis, and old intestinal tuberculosis. Twenty-eight other cases observed by the author showed tuberculosis of the thoracic duct twelve times: (girls, 12, 23; man, 21; two men, 22 and 42; woman, 53; men, 64, 66; two women, 66, 68; man, 68; man, 81 years of age); erosions of pulmonary veins 6 times: (child 1 year old; girl, 2; two girls, 7; one 10; man 45); multiple tubercles of the intima of pulmonary veins in 10 cases: (girls, 16 months, 6, 7, 10 years, also with isolated tubercles of the aorta; women, 30, 34, 54 years old); one case of rupture into the jugular (21 year old man); and one case of rupture of cardiac tubercle into the auricle with ulceration of the valves of the pulmonary artery, (2 year old boy).

Wherever the bacilli are located they may cause typical endothelioid cell—giant cell—submiliary and miliary tubercles, in the interstitium, in the septa, peribronchial or perivascular tissue.

As a rule, tubercles quickly extend to adjacent alveoli easily recognizable by elastic fibre staining; at the same time, the tissue changes may remain predominantly productive. The tubercles enlarge and their centers caseate. Exudative processes may or may not appear in the alveoli and a complete granuloma nodule is formed containing giant cells and surrounded by a fresh, often relatively broad, pneumonic circle. Most miliary tubercles, especially the larger ones, are probably built microscopically in this manner (chiefly those in the upper lobe).

As emphasized by Orth, the older the tubercles, the more the elastic fibres of the original tissue disappear.

At another time, the organisms at once stimulate the formation of cellular alveolar pneumonic foci within which the alveoli and bronchioles are filled by exudate; a quiet development of typical tubercles does not take place. These pneumonic foci usually caseate quickly and appear on section as prominent granular nodules, rounded or angular, of unequal size but mostly larger than miliary.

When such foci become chronic, the nodules caseate or undergo hyalin or fibrous changes, and the condition is spoken of as chronic miliary tuberculosis.

Not rarely, in the region of miliary tuberculosis of the second kind, the walls of the smaller bronchi are destroyed by caseation and adjacent arteries may show both tuberculous infiltrates in their walls and thickenings of the intima; internal rupture of extravascular miliary foci into veins is also seen (comp. Beyman, lit.).

**Macroscopic Appearance of the Lung of Miliary Tuberculosis.**—The organ is somewhat distended, vascular, sometimes slightly edematous, air-containing, finely granular to palpation. The section surface is dense, and covered evenly with hard, prominent nodules intimately and inseparably incorporated in the lung tissue; they are approximately as large as millet seeds, but may be smaller, or larger from confluence (conglomerate tubercles), (fig. 189-a and b). Many are submiliary. The youngest, smallest, approximately round nodules are semi-transparent, grayish white, more easy to palpate than to see (oblique illumination!); larger nodules are more opaque, some have yellow centres, (caseation), but the process causes death so quickly that extensive caseation seldom develops. The nodules are usually larger in the upper lobe than in other parts and caseation progresses further; doubtless they grow more rapidly there (Orth, the author, Ribbert, Tendeloo, etc.). It is interesting that certain local conditions seem able to protect a portion of the lung from invasion,

*e.g.*, pressure of an exudate, or pleural adhesions, (see Schmorl, Hedinger, lit.), and such an area escapes the general miliary tuberculosis. The nodules may bulge into the pleura and also extend to it, but usually the pleura is smooth, except, perhaps, for a spotty fibrinous coating. Miliary tuberculosis may appear in an intact lung, or in one which already contains chronic tuberculous changes.

In the general miliary type, the nodules are found in other organs also, especially the liver, spleen, kidneys, serous membranes and occasionally the heart muscle, endocardium, intima of aorta (rare), thyroid, etc.

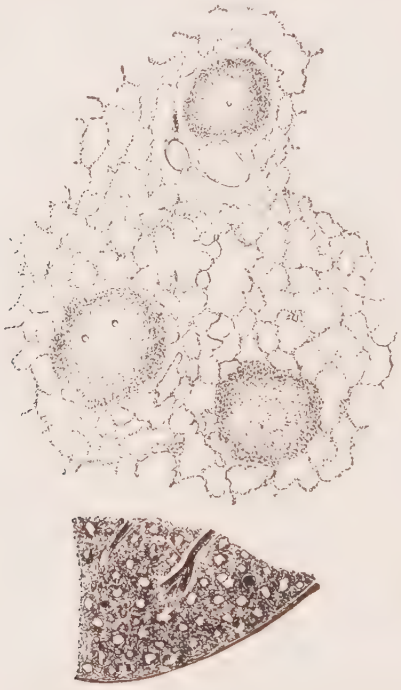


FIG. 189.—a and b, Hematogenous miliary tuberculosis of lung; three miliary tubercles; one contains two giant cells, the others one each. The macroscopic picture shows a piece of lung with miliary tuberculosis; nat. size.

Tubercles of the choroid are not rare, first described by Cohnheim and Manz, and clinically of value in the diagnosis, which is often quite difficult. Acute miliary tuberculosis is occasionally observed in conjunction with pleuritic exudates, genito-urinary tuberculosis, tuberculous bone and joint affections, especially after operative procedures (Volkmann). The organisms have repeatedly been demonstrated in the blood during life in cases of the miliary form (comp. under blood, p. 213) (clinical by Cornet).

Partially disseminated hematogenous miliary tuberculosis may develop in the lung from rupture of a caseous plumonary focus, or a primary tuberculosis of a bronchial lymph node into a branch of the pulmonary artery.

When the organisms enter the lung from a tuberculous focus in lymph nodes, intestinal tract, bones, etc., they favor the cranial parts; disseminated foci are established only to a slight extent in the scaffolding, but mostly about bronchioles from which they spread further.

Secondary pulmonary tuberculosis presupposes a primary infection in some other part of the organism, or in the lung itself. Most frequently, this is an aerogenous new infection, *i.e.*, a reinfection. In reference to the peculiarities in the anatomical changes and the altered reaction of tissue resulting from the previous primary infection, see p. 454 (allergy, reaction changes, anaphylaxis, increase of sensitivity, etc.).

Not every tubercle bacillus entering the lung causes tuberculosis nor does the passage of bacilli into the blood stream necessarily lead to miliary tuberculosis; even if a consumptive showed some organisms in his blood during life, which is not rare (p. 213), the autopsy may show no miliary tubercles; indeed, as a rule, they are absent. Perhaps a certain larger number must circulate in the blood under certain conditions, *e.g.*, rupture of a large caseous focus, etc.

Many questions are still open; see Aufrecht, von Baumgarten, Ribbert and others. First of all, are the lungs frequently or usually involved secondarily, and by the lymphogenous or hematogenous route? Is the infection carried there from the intestines, through the walls of which the organisms pass either directly, or through lymph nodes, and then into the blood and lymph (Klebs, Calmette, Schlossmann); or, as in the experiments of J. Koch and Mollers, do the organisms reach the lungs by the lymphogenous route from the bucco-pharyngeal cavity and thus cause a chronic localized tuberculosis in the upper lobes? Does the inhalation of tubercle bacilli from the air, as expressed by Kretz, cause a general infection which is finally localized in the lung? Is infection hematogenous from some distant focus; or as assumed by Weleminsky, does it develop from an older tuberculosis of a lymph node; or, as believed by Ribbert, in his lymphatic-hematogenous hypothesis, are the lungs which escaped infection by inhalation involved secondarily en retour from the bronchial lymph nodes which are primarily infected? Without doubt, hematogenous foci may resemble inhalation foci, *e.g.*, from a tuberculous urinary bladder (see Orth), but this is apparently rare. Among other things, it might be said against Ribbert's theory, that caseous or chalky foci in bronchial lymph nodes are found much more frequently in obsolete than in florid pulmonary tuberculosis, while, according to his theory, the reverse should be the case. Schmorl decidedly objected to it, and many other investigators also (lit. in appendix); they support the old opinion of direct aerogenous infection as the most important practical form of tuberculosis; Baumgarten points out the difficulty of making any certain statements in

reference to the point of entrance, requesting us to consider all possible avenues with equal care. In animal experiments, especially those of Flugge and his pupils (lit. in appendix), it was demonstrated conclusively that the idea of inhalation infection is far more logical than other theories, especially the intestinal.

**Lymphogenous Tuberculosis.**—Tubercle bacilli may reach the lungs through the lymphatics, *e.g.*, from a tuberculous bronchial node after rupture of its capsule, or from a carious rib or from caries of the spine. Dissemination then occurs, often of miliary tubercles, which reveal by their grouping the close relationship to their point of origin.

Straub and Otten contrast this form, which starts from the nodes of the hilum, with predominantly unilateral infection starting from the apices.

Infection of bronchial nodes may occur in various ways: from older pulmonary foci from which infection reaches the nodes, or organisms pass through the lungs without causing local infection, and are retained, or the first organisms reach the intestines with the food (milk), as assumed by Klebs, then enter the mesenteric nodes and from there the bronchial nodes. Most authors, however, believe there are no such lymph channels. Others assume that the organisms arrive from the buccal and pharyngeal cavities, especially from the tonsils, and from there (*a*) by way of the lymph vessels, pass to the parietal pleura and then to the apices of the lung (comp. Volland, Wassermann, Grober and others), but Beitzke and Most could not show this with injections in animals, although J. Koch and Mullers did in two cases; or (*b*) from the cervical lymph nodes, they enter the bronchial chain and from there the lungs. Harbitz thinks such a relationship is possible between the cervical and bronchial lymph nodes and indeed considers this the chief route of infection in the pulmonary tuberculosis of children (comp. v. Hansemann). Although Most could not demonstrate such a correlation under normal conditions, he admits it is possible in pathological conditions. On the other hand, Beitzke, in opposing the above views, attempted to prove that the cervical lymph nodes of children are infected from the bronchial nodes or from the mouth, since the bronchial nodes almost without exception show the more severe changes; they are nfected from the lung as a rule, or from the bronchial tree, which are then considered the portals of entry. The author can interpret his own experiences in the same way. (Comp. Kovacz, Hart, Beitzke, Albrecht, Ghon, Hedren.)

Distribution by the lymphatics and the appearance of disseminated tubercles wihhin the lung occur very frequently when a focus is already present, seen especially in children, when the process is both acute and extensive. In the chronic pulmonary tuberculosis of adults, further

extension occurs almost exclusively by way of the lymphatics (see under peribronchial and perivascular tuberculosis).

**Aerogenous Tuberculosis. Inhalation Tuberculosis.**—This is at first quite circumscribed usually near the apex and is designated initial aspiration tuberculosis. The selection of the apices (and the bronchi, see p. 349) for the spread in adults is due to their greater vulnerability in consequence of relatively poor blood supply (impaired nutrition of tissue due to deficient vascularization on account of slight pressure fluctuations, Hofbauer), and on account of imperfect ventilation (Hasse) due to lack of space for the apices to grow, especially the right, particularly during puberty; the development of the bronchi and the parenchyma is hindered, and unfavorable mechanical conditions for respiration are created. According to Tendeloo, the energy of movement of the lymph is at its lowest in the apices during inspiration and expiration, and this is favorable for the lodgment of tubercle bacilli, dust, and other foreign substances.

In the lung of the suckling this unfavorable topography is not as yet present except probably in areas mentioned on p. 436 (Tendeloo, Peiser). According to W. A. Freund and Schmorl, Hart, early ossification and shortening of the first costal cartilage with constriction of the apex (Schmorl's lung pressure furrow) is supposed to predispose to the colonization of organisms (comp. opposed Peiser); indeed, the formation of a joint on the first rib was believed to be essential for the cure of an apical tuberculosis (s. Jungmann). But the anatomical teachings of Freund were not borne out by the investigations of W. H. Schultze, Ulrici, and Sumita and Sato from the author's institute (see also H. Virchow, Wolff-Eisner, O. Meyer). Bacmeister's experiment, however, apparently proved Freund's teaching of aperture stenosis; he constricted the upper thorax and vicinity of rabbits by wire and succeeded in demonstrating a predisposition of the apex to both aerogenous and hematogenous infection. But these experiments are technically too imperfect to serve as a support of Freund's theory which emphasized the shortening of the first rib; they do show, however, that changes in the blood and lymph circulation favor colonization in the same way, *e.g.*, as in observations of Serog and Hart, viz., compression of the lung by a tumor, *i.e.*, an aneurysm. But Iwasaki, under the author's direction and using better technique (artificial stenosis by resection of a part of the first rib), showed that such stenosis of the thoracic aperture caused by shortening of the first rib does not really predispose the pulmonary apex to tuberculosis.

The question in reference to animal experiments is thus in this situation (see Bauer also). Moreover, Freund's theory has met with much opposition from the clinical side (Wenckebach, Sorgo, W. Neumann), although Hart still clings to his own and to Freund's opinions.

At all events, the apices may be considered the most frequent starting points of chronic tuberculosis of the lung (phthisis), at least in adults; in children (comp. p. 455) there is rather a predilection of the hilum and the dorsal and paravertebral parts in which the primary infection shows the same common forms of infection. Then during the course of phthisis, the respiratory channels play an important part in its spread. The right lung is more frequently diseased (consult A. E. Mayer).

**Where Do the First Pulmonary Foci Develop?**—Apart from the relatively rare case mentioned on p. 349, aerogenous tuberculosis localizes first in a medium size or small bronchus.

There is practically unanimous agreement that the primary point of attack is where the bronchi pass into respiring parenchyma, *i.e.*, in the finest intralobular bronchioles and end bronchi. The process may begin within the bronchioles, first in the mucosa, and then spread to the infundibuli and alveoli (tuberculous lobular pneumonia). But it is also thought that tubercle bacilli may enter the alveoli directly, or that they may locate first in the lymphatics of the interstitial tissue in the vicinity of the end bronchi, from which they spread to the air channels. Then an interstitial nodular lymphangitis results, the so-called peribronchial tuberculosis.

Since, naturally, it is very rare to discover a just beginning primary focus in the lung, deductions must be made in reference to initial tuberculosis, both from examinations of fresh areas which are encountered often enough in the course of phthisis, and from animal experiments.

In the experiments conducted by Watanabe and Herxheimer, with injections of bacillary suspensions, the organisms first attacked the alveolar epithelium and Herxheimer describes their injurious necrotizing action on this and the elastic fibres, followed by proliferation of fixed elements, epithelium and connective tissue cells. The first macroscopic foci develop by continuity from the first foci, or by way of the bronchi or lymph channels.

It is then a focal tuberculous peribronchitis, or focal caseous bronchopneumonia, the latter especially in children, or a caseous nodular affair.

The fate of the first foci varies; fibrous proliferation encapsulates and heals them (more details in next paragraph), or they become the starting points of various forms of chronic tuberculosis which extend continually, or after remaining stationary for a time, become progressively active again. Thus the primary focus may heal, but during its activity, secondary foci are established in distant parts or organs, *e.g.*, hematogenous route may send the organisms into other parts of the lung causing new secondary pulmonary tuberculosis (see p. 454). Furthermore, even after healing, an aerogenous new infection may take place which is perhaps the more fre-

quent event. See dissertation of Rankel, p. 454, in reference to the variety of processes in the lungs in primary and secondary (also tertiary) tuberculosis.

The picture of chronic tuberculosis of the lungs is so variable that it may be said no two tuberculous lungs are alike. In a number of cases, the alveolar parenchyma and the bronchi participate, and inflammatory exudation plays the prominent part, *i.e.*, tuberculous pneumonic changes. The caseous products may quickly liquefy, be distributed by way of the bronchi and infect larger areas. At the same time, dissemination (absorption) through the lymphatics takes place. In other rarer cases, the alveolar parenchyma remains comparatively free of disease, and the process shows a tendency to creep along peribronchial and perivascular lymphatics with the formation of nodules in the interstitial tissue. Again, in other cases, caseous bronchial processes and peribronchial proliferation are combined and may stimulate exudative processes in their own and adjacent alveolar territories. Then there are caseous bronchitis, and nodular pneumonic changes so frequently seen in so-called tuberculous peribronchial foci. The picture in some cases is further modified by softening of caseous masses and cavity formation which remain entirely absent in others; indurative healing processes due to reactive connective tissue proliferation develop in the vicinity of formations in some lungs; in others none occur. If very active connective tissue proliferation sets in, the progressive changes may be checked and many places of smaller and even larger extent undergo cicatricial healing.

These suggestions make it clear that phthisis may completely destroy some lungs in a few months, or may heal in time, or allow the patient to live to very old age.

The terms "phthisis" and "pulmonary tuberculosis" are frequently used as synonyms, but the process should be called, at least, tuberculous phthisis, so that this term is used only in cases in which the loss of lung tissue is due to a tuberculous process. The attempt to introduce the term "phthisis bacillus" (Aschoff) instead of tubercle bacillus cannot be sufficiently deprecated, (see Orth, Lubarsch and others).

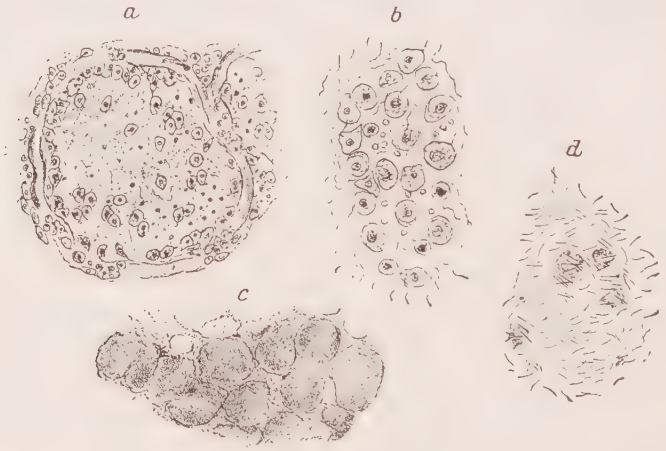
The most important anatomical forms will now be discussed.

**Tuberculous Pneumonia.**—In every stage of pulmonary tuberculosis, from the very beginning, changes may develop in the alveolar parenchyma which are named according to the extension of the process, miliary—sublobular—or lobular tuberculous pneumonia. Two anatomical forms are differentiated:

(*a*) **Caseous Pneumonia.**—The presence of tubercle bacilli in the alveoli causes an exudative inflammation accompanied by proliferative processes, giving a picture very similar to that of other pneumonias, especially the

catarrhal and fibrinous. But the difference between tuberculous pneumonia and the others is caseation. According to its course, it is divided into acute, subacute and chronic.

Microscopically, acute caseous pneumonia is characterized by both active exudative and proliferative processes. In the alveoli, there is a viscid, glassy albuminous exudate in which thready fibrin is contained in larger quantities as emphasized first by Orth. The striking cellular elements, in addition to poly- and mononuclear leucocytes and red blood corpuscles in varying numbers, are of epithelial character. This proliferated and desquamated alveolar epithelium is not easily distinguished from large lymphocytes (Orth) when it becomes rounded in the exudate into trans-




FIGS. 190 to 193.—a, b, c. Tuberculous pneumonia; a, alveolus with cellular exudate; cellular proliferation in wall (med. magn.); b, cells in fibrinous exudate (high power); c, alveolar complex with caseous hepatization and cellular interstitial tissue. Alveolar structure still recognizable (low power); d, tubercle bacilli at margin of a caseous focus (oil immersion).

parent cells with pale vesicular nuclei (figs. 190 to 193-a and b), but lymphocytes have relatively small dark nuclei. Marchand considers most of them swollen alveolar epithelium, (see also Milian). They may contain pigment, and sometimes the whole exudate filling the alveoli with loose plugs seems to consist of these cells. Numerous bacilli are always present. The process must be considered due to the entrance of many bacilli and much toxin because both proliferation and exudation appear. In the subacute and chronic caseous pneumonias, the proliferative processes are more apparent, but bacilli are found in the periphery of the caseous nodules, and also perhaps in enormous masses in the young cellular, tuberculous tissue (comp. p. 423, histology of the tubercle). Later, everything undergoes caseation into a finely or coarsely granular, amorphous, nuclear debris (caseous hepatization). In the beginning, the alveolar septa are unchanged, but as the contents begin to caseate, the septa are infiltrated

and proliferative processes appear. Since the elastic fibres are preserved, the alveolar boundaries are visible for a long time, although the contents, including the framework, are changed. When the caseous mass softens, the elastic fibres are finally detached and the alveolar framework collapses. The capillaries in the alveolar walls are hyalinized and occluded even in the beginning, and in more chronic cases, adjacent arteries are occluded by simple endarteritis or by caseous proliferations.

Sometimes part of the alveolar exudate escapes caseation, and is organized to simple carnification as in fibrinous pneumonia (comp. p. 398), or tuberculous granulation penetrates the fibrin-filled alveoli (tuberculous carnification) and then undergoes cicatrization or caseation (Ceelon).

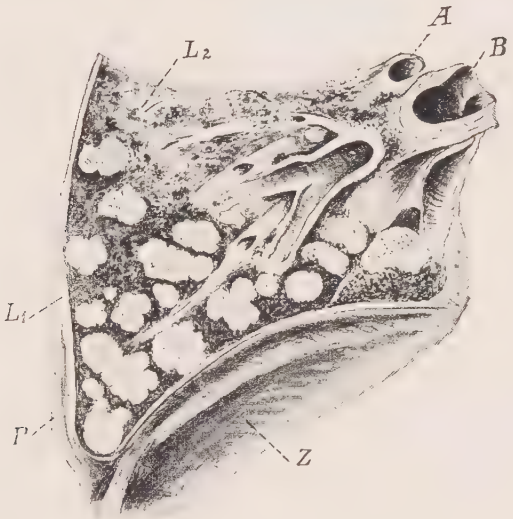



FIG. 194.—Nodular firm caseous lobular areas in lower lobe, embedded in slaty indurated tissue (Ll). $L_2$, air-containing pigmented lung tissue; A, pulmonary artery; B, bronchi; P, adhesions of pleural surfaces; Z, diaphragm adherent to pulmonary pleura. $^9/_{10}$ nat. size.

Macroscopically, the caseous pneumonic areas are grayish red at first, and then yellowish white, opaque, dry, airless, slightly raised and somewhat granular. They are of miliary size when a few alveoli are involved, or lobular or confluent or extensive like the lobar hepatization of common pneumonia (fig. 199-k). The hepatized parts gain in volume and weight, and the author found one lung weighing 2570 grams. At this point, the differential point from croupous pneumonia is the dry firmness of tuberculosis.

Caseous pneumonia may spread very quickly over large areas (acute caseous pneumonia), and by softening and cavity formation lead to rapid destruction of the lung (phthisis florida, galloping consumption). Mixed infections play an important part (comp. p. 428). A wide zone of gelati-

nous lung tissue is often present around caseous portions. In subacute and chronic cases there is little tendency to softening, so that stiff caseous lobular masses are found around which the lung tissue is cicatrized or indurated (fig. 194, see above).

**Smooth Pneumonia or Gelatinous Infiltration.**— This condition produces a grayish red, glassy, gelatinous exudate in the alveoli surrounding larger or smaller caseous foci, or, in larger portions of the lung, an airless, grayish red gelatinous consolidation with all the physical signs of apparent lobar distribution (A. Frankel). Microscopically, the most striking detail is marked congestion and especially exudation of serous, and to a less extent, fibrinous materials; cellular admixtures (desquamated swollen epithelium) are relatively sparse. Bacilli are not found, as a rule, and other bacteria were not demonstrated by A. Frankel and Troje. But other cases occur in which numerous tubercle bacilli are found (comp. the next paragraphs). If the gelatinous infiltration undergoes caseation, grayish yellow stippling and foci appear in the glassy tissue as well as more fibrin and fat droplets (also doubly refracting granules) in the desquamated epithelial cells.

According to the investigations of Baumgarten, A. Frankel and Troje, it is probable that this exudation is an effect of the toxic products of the organism. When caseous foci containing numerous bacilli are found within the gelatinous infiltration, it is easy to believe that their toxins are distributed to the surroundings (analogous to the action of tuberculin). Therefore, it is not surprising that no organisms are found in the gelatinous parts, which is considered the rule by A. Frankel and Troje. When many are found, it is possible that they and much toxin reach the parenchyma by way of an open bronchus. Thus in the beginning, the acute exudative effect of the toxins predominates, while proliferation of the epithelium sets in later, and, of necessity, caseation processes, which are not at all necessary in non-bacillary gelatinous infiltration, and which indeed may disappear by absorption. But if gelatinous infiltration is followed by caseation, the bacilli were present at the very beginning or arrived later, and proliferative processes also went on. This shows that there is no justification in considering gelatinous infiltration merely a precursor of caseation (comp. non-appearance of caseation, pp. 425 and 427).

Naturally, when caseous foci enlarge, the proliferation with subsequent caseation extends to the gelatinous surroundings.

But common true pneumonic changes may also be induced in the vicinity of tuberculous foci if the proper organisms are present (streptococcus pyogenes, diplococcus pneumonia), as assumed, especially in the extensive diffuse infiltrations in the various forms of tuberculosis. In other words, the infection is mixed, and its importance to the tuberculous process

is discussed on pp. 439 and 447. It should also be mentioned that Tendeloo thinks of the possibility of hematogenous origin in bilateral caseous pneumonia, and he speaks of general focal tuberculous necrosis.

The small, so-called bronchopneumonic foci so frequently found in the lower lobe, deserve especial consideration. They develop from the aspiration of bacilli, and groups of bronchioles or atria are simultaneously infected with their alveoli and adjacent parts. Thus the groups of caseous foci are in the shapes of shamrocks or bifurcated, corresponding to the branches of an end bronchus (as a rule into 3 branches) which

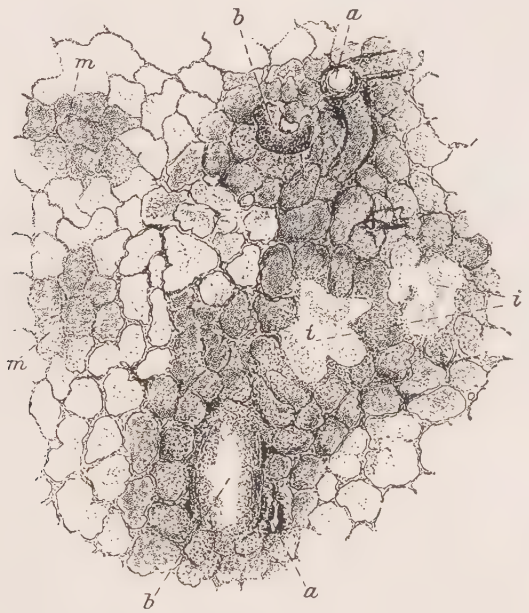



FIG. 195.—Caseous bronchopneumonia in lower lobe from aspiration. b, caseous bronchitis and peribronchitis; a, branches of pulmonary artery narrowed by endarteritis and tuberculous proliferation, surrounded by coal pigment; i, infundibulum cut diagonally; m, miliary tuberculous pneumonic foci of aspiration (low power).

sometimes show a most minute lumen in their centers. Of course these lumena are often invisible because filled with caseous material and then the foci give the impression of solid nodules.

To be strictly correct, in most cases, it is not merely a caseous pneumonia which progresses within the air-containing parenchyma belonging to a bronchiole, infundibulum and alveolus, but also a caseous peribronchitis and peribronchial pneumonia which extends through the walls of the bronchioles into the adjacent interstitial tissue and from there to the nearest alveoli (fig. 195).

These foci are often called "acinous" as suggested by Nicol, but Ribbert denies that it is a constant involvement of a unit called "acinus,"

indeed, denies that the process is confined chiefly to the bronchiole and its vicinity. According to him, an "acinous phthisis" in Nicol's sense does not occur any more than an acinous nodular phthisis.

When the foci become older, their peripheries undergo more fibrous changes (see p. 439) which may be important, while the central portions remain caseous. The foci become firm, white or light gray. Isolated giant cells may be present (fig. 196-r), in the cellular, fibrous peripheral zone (fig. 196-f). Within the central caseous portion (K), blood vessels are occluded. Since the lymphatics also are blocked, coal pigment may still be carried in, in the beginning, but cannot get out and remains permanently

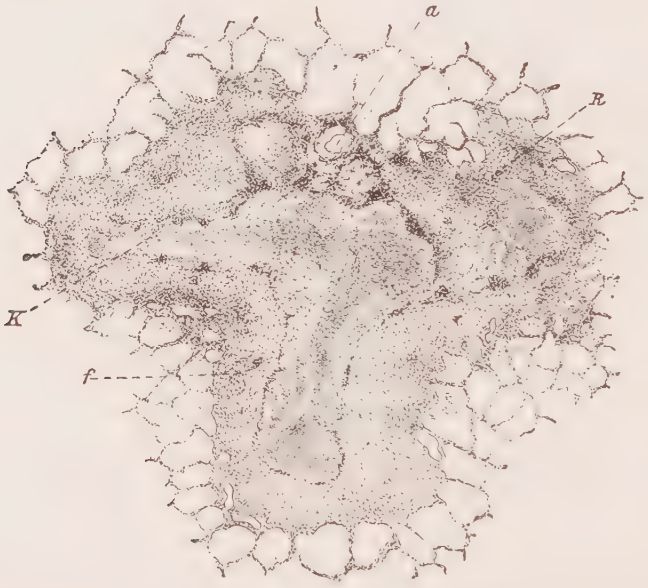



FIG. 196.—Clover-leaf-like, older caseous-fibrous bronchopneumonia due to infiltration of alveolar tubules and adjoining alveoli. K, caseous center corresponding somewhat to the ramification of the alveolar tubules, caseous masses surrounded by coal pigment; f, cellular, fibrous periphery with occasional giant cells; (R), cellular fibrous thickening of the septa. a, artery.—Alum carmine stain; (low power).

to faintly outline the former tissue boundaries as in the preparation, fig. 196. The topographical relation of the caseous fibrinous bronchopneumonic foci to the pulmonary artery is of importance since they always rest closely against its branches. The arteries are very frequently changed by productive endarteritis or by tuberculous, often caseous, proliferations.

As a rule, there is much coal pigment in the vicinity of the arteries (p. 419). Generally speaking, the caseous fibrous bronchopneumonic foci are without lumena, like solid nodules, which differentiates them from peribronchial tuberculosis (see next paragraph).

**Peribronchial and Perivascular Tuberculosis.**—This condition is also called tuberculous peribronchial and perivascular lymphangitis and perilymphangitis (nodular), or, in brief, "tuberculous peribronchitis."

When organisms enter the lymph vessels of the interstitial tissue from a tuberculous focus already present, or from the alveoli, or by passage through the wall of the bronchioles, the nodules produced by their activity are located chiefly where the finer lymph spaces of the interalveolar parenchyma are collected, *i.e.*, at the transition of the alveolar ducts into bronchioles.

There then appear isolated, miliary, lymphogenous tubercles, or groups or chains of nodules, which surround the bronchioles and small bronchi, the lumena of which can usually be recognized macroscopically as tiny holes or clefts. Since the nodules are strung along the course of the lymphatics, the process extends from one end bronchus to another, forming shamrock-like or rosette-shaped foci (see fig. 197 below).

It is not strictly correct to call these foci simply "tuberculous peribronchitis" according to their macroscopic impression; a better name is "peribronchial and perivascular tuberculosis," but the microscopic examination teaches that the tuberculous proliferation very frequently extends to the alveolar septa and alveoli (tuberculous pneumonia), as also to the bronchial walls (tuberculous bronchitis), which become partially caseous or are changed into caseous or caseous-fibrous rings (fig. 198-c).

Tuberculous peribronchitis may also develop by extension of tuberculous bronchitis directly through the wall into the vicinity. In their further course, the tubercles spread over larger areas and eventually encroach upon the largest part of a lung.

Chronic nodules may undergo partial or total fibrosis into so-called fibrous tubercles (chronic fibrous peribronchial and perivascular tuberculosis). Since the individual tubercles fuse with the connective tissue, the hard nodules are sometimes as large as a pea, but have caseous centers and fibrocellular peripheries perhaps containing many giant cells (fig. 198).

The lung tissue between thickly grouped foci is consolidated by fibrous induration and pigment, or by simple collapse.

Carnification is also important. See p. 439.

In some chronic cases the peribronchial tuberculosis retains its original interstitial character throughout its further course. In other cases, the adjacent alveoli are promptly involved and a wide spread tuberculous pneumonia is developed.

While the combination of caseous bronchitis and peribronchitis is usually seen in small areas, it nevertheless occasionally assumes larger dimensions. It must be remembered that it may be caused either by

FIG. 197.—Tuberculosis of lung (above process very old, below more recent). Fibrous and slaty induration of lower portion of upper lobe, and upper portion of lower lobe. Bronchiectasis in cicatricial tissue (f); numerous rounded caseous foci (one at d); c, and e, irregular bronchiectatic cavities partly lined with mucosa, partly ulcerated; e, shows tendency to cicatricial contraction. In lower part numerous "peribronchial tuberculous foci" in groups, sometimes assembled in figures like trees. The dark dots and striae within the foci are bronchial lumina cut across and lengthwise. At b, the foci lie close together and pass into the cicatricial indurated tissue without definite boundaries in the vicinity of some foci, e.g., a lung tissue partly atelectatic, dark; g, adherent cicatricially thickened costal pleura; h, bronchi; i, anthracotic lymph nodules; $^{9}/_{10}$ nat. size.

aspiration of bacilli or by invasion from the vicinity (tuberculous artery, interstitial tubercle, comp. p. 429). When somewhat larger bronchi are filled with caseous material and their walls and surroundings also are uniformly caseous, their cross sections appear like broad, smooth, caseous rings or nodules, sometimes with visible central holes or depressions, while longitudinal sections reveal more or less thick, cheesy branched strands containing the quite irregular, often remarkably wide, lumena of disintegrated branches.

Rupture of a caseous bronchial lymph node may also initiate caseation of the bronchus involved.

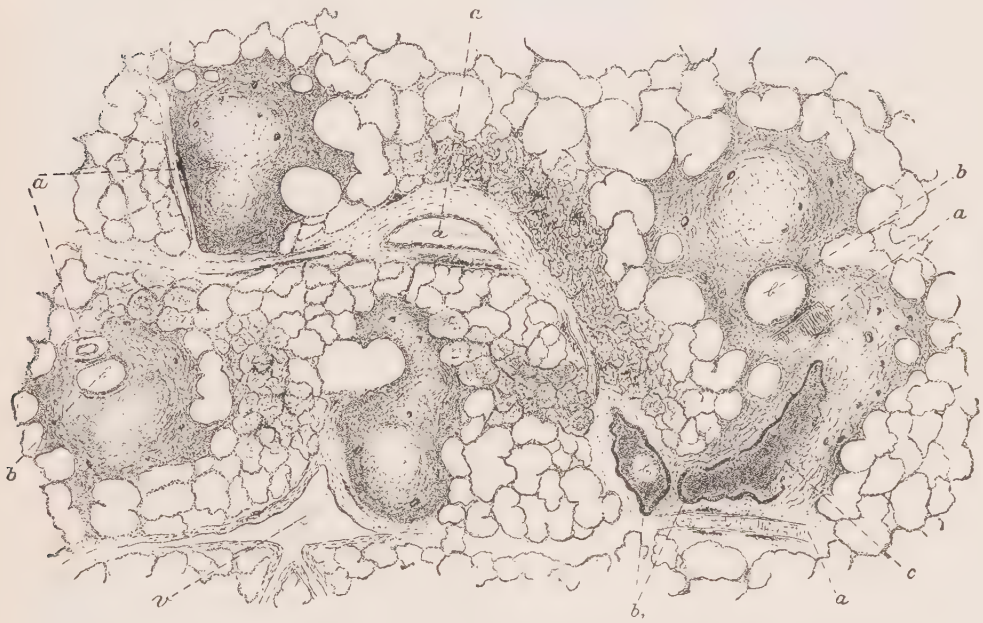



FIG. 198.—Chronic peribronchial and perivascular tuberculosis, from a case of chronic phthisis. a, arteries surrounded by pigment; to the right, a particularly caseous artery; v, vein; b, bronchi. At C tuberculous tissue has proliferated through the bronchial wall; bl, bronchi with preserved cylindrical epithelium, caseous suppurative masses in lumen. The peribronchial and perivascular tuberculous foci are caseous in centers; the cellular periphery is plainly fibrous here and there and contains numerous giant cells. The lung tissue between is partly indurated, partly pneumonic, most of it edematous; (med. magn.).

Macroscopical differential diagnosis of (*a*) caseous bronchitis and peribronchitis, (*b*) tuberculous peribronchitis and (*c*) nodular bronchopneumonia.

In caseous bronchitis and peribronchitis in which the degenerated branching strands and rings appear on the section surface, careful rinsing with water sometimes washes away the bronchial contents and reveals the former bronchial lumen dilated and irregular from caseous disintegra-

tion. This is usually sufficient for differentiation from peribronchial tuberculosis, *i.e.*, if the latter is confined chiefly to the lymphatics. The chains of nodules surround the bronchial lumen and narrow it so that, sectioned in its long axis, it appears as a sharply outlined narrow cleft and on cross section as a small dot. Small caseous or caseous-fibrous bronchopneumonic nodules are, as a rule, without lumena, the latter similar to firm solid nodules, the former sometimes alveolar and granular. In caseous bronchitis and peribronchitis the caseation is usually earlier and more uniform than in peribronchial tuberculosis, and the masses appear smooth and regular on section. In peribronchial tuberculosis, however, the section surface is nodular, because the individual tubercles and tubercle groups are still relatively well confined; if the tubercles are old, they are whitish gray, hard nodules, usually of macroscopic size, often not caseous, and frequently actually fibrosed (p. 425).

If these points of differentiation (to which, indeed, more might be added) apply to typical areas, the character of minute foci is sometimes to be determined microscopically only, and even then, diagnosis may not be easy.

**Changes in Tuberculous Foci and Their Surroundings.** (*a*) **Softening, Cavity Formation.** (*b*) **Indurative Processes.**—(*a*) Softening, disintegration, cavity formation.

The cavities to be discussed, formed by (1) liquefaction and sequestration of caseous pneumonic areas, are the most important, although not the only form of cavity.

There are in addition cavities formed by (2) endo- and peri-bronchial caseation, described on p. 348, and (3) tuberculous ulcerative bronchiectatic cavitation (see p. 353). Ranke also mentions those due to rupture of caseous lymph nodes into bronchial lumena, but these are relatively rare. The stiff caseous masses in the various tuberculous processes, especially in caseous lobular pneumonia, may begin to liquefy, generally in their centres and finally resolve into puriform pulpy debris. The thin molecular fluid contains elastic fibres separated from their tissue, isolated yellow grumous particles, or large lumps of dead caseous tissue and usually very numerous tubercle bacilli. Leucocytes are always present. Wherever liquefaction takes place, a cavity remains, at first closed and surrounded by caseous tissue, (cavern, vomica, lung abscess). Cavities therefore do not develop by enlargement of a preformed space, but by disintegration of lung tissue, although a bronchiectasis may change into a cavity if its walls are destroyed by tuberculous ulceration (comp. p. 353), (bronchiectatic tuberculous ulcerative cavity).

When small cavities coalesce by peripheral progressive caseous disintegration, large bulging holes develop in a surprisingly short time.

The size and form of early cavities depend entirely on the caseous focus from which they develop. If they arise from a peribronchial focus or a small area of bronchopneumonia, the cavity is, of course, very small at first, and more or less rounded and circumscribed; but if they appear in a caseous pneumonic area of lobular, or lobar dimension, then multiple, more or less diffuse, liquefaction foci are present from the very beginning with peculiar tissue tears; their confluence promptly forms an extensive, irregular system of cavities which contain a thin material, sometimes foul smelling, and mixed with caseous fragments. Not rarely, one or more lobes are practically excavated in a very short time, but if the liquefactive process is not so extensive and is confined to the margins of the caseous mass, then large caseous portions are detached, like sequestrae. In a 15 months old girl, the author saw a caseous sequestrum the size of a chestnut almost filling a cavity. The fact that interstitial tubercles show less tendency to softening, makes it probable that softening is more likely to occur in the presence of mixed infection which is always found in the buccal cavity and sometimes in the respiratory channels. But the number of tubercle bacilli probably modifies the softening because enormous numbers may be found in the smallest, just developing, cavities which are not yet in communication with bronchi. When, however, caseation is combined with tissue suppuration, sequestration or liquefaction, other pathogenic organisms are probably always present (mixed infection).

Cavities prefer the apices of both the upper lobes, and the lower lobes. Fresh cavities are surrounded everywhere by caseous material. The larger septa, and especially the vessels, resist progressive disintegration and are the chief constituents of the ragged framework which is seen in fresh cavities and which is still partly preserved in quite old ones (fig. 203).

When cavities rupture into bronchi, the bacilli-containing material is emptied and expelled with the sputum which exposes the upper bronchi to infection, and other lower, perhaps healthy, parts of the lung to aspiration. Also, other bacteria have an opportunity to enter the cavities through the bronchial tree (secondary or mixed infection).

The organisms concerned are usually streptococcus pyogenes, staphylococcus pyogenes, aureus and albus, pneumococcus, micrococcus tetragenus, b. coli, influenza bacilli, etc. Since they multiply in the cavities which have been called "incubators," they accelerate the decomposition processes. The contents become purulent or necrotic, and the pus formation causes sequestration of caseous masses, but at the same time, this hastens clearing of the cavity, *i.e.*, curative tendencies. On the other hand, by aspiration, fibrinous, suppurative, hemorrhagic and necrotic processes may be developed in bronchi and alveoli, thus accelerating the phthisical process.

Their effect on the fever of phthisics is still disputed; at any rate, it is not due to invasion of the blood by these bacteria as a rule (Jochmann), (see pp. 427 and 440).

When a cavity remains stationary for a time, a wall of reactive granulation tissue develops from the neighborhood. This wall actively pro-

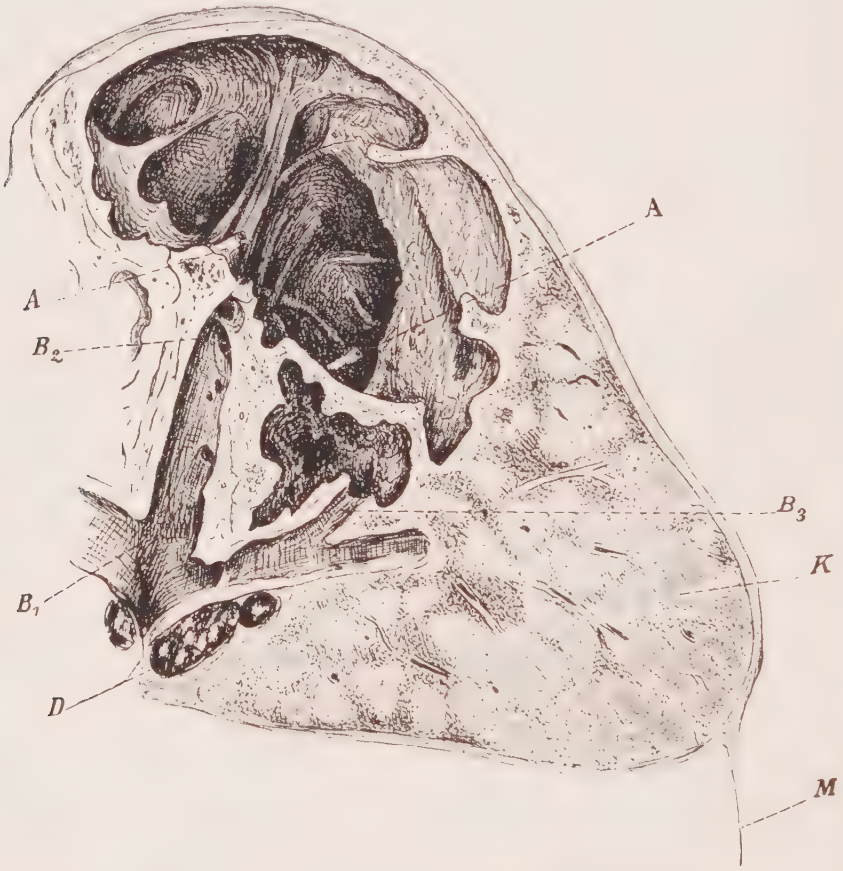



FIG. 199.—Large cavities in upper lobe; the largest, communicating with bronchus $B_2$ is fairly old; caseous fibrous lung tissue in vicinity; the bronchus $B_3$ leads into a smaller, more recent cavity communicating with the main cavity. At A, vessel stumps project into the large cavity. The rest of upper lobe occupied mostly by lobular, confluent, caseous pneumonic foci K; only few remnants of air-containing parenchyma; $B_1$, bronchus near hilum; D, anthracotic tuberculous lymph nodes; M, middle lobe; pleural surfaces adherent; $^9/_{10}$ nat. size.

duces pus. But if the granulation tissue contains tubercles which enlarge and undergo caseation and if the wall also becomes purulent, the cavity grows larger (chronic progressive cavity). They almost always assume a spherical form. In the caseous wall the organisms are usually the tubercle bacillus exclusively, often in enormous numbers.

While this form of chronic progressive cavity formation may be called caseous ulcerative, or tuberculous ulcerative, or specific ulcerative, some chronic progressive cavities in time may be spoken of as simple ulcerative, because the inner surface is covered by a thin pyogenic membrane which stains poorly, and caseous material and bacilli are then absent. Progressive enlargement of the cavity is accomplished only by secondary non-tuberculous, non-specific, suppurative, ulcerating inflammatory processes.

When a cavity remains stationary, on the other hand, the granulation tissue ceases to be tuberculous and to ulcerate, and changes into cicatricial connective, sometimes cartilaginous tissue which lines the cavity smoothly (fibrous, healed cavity). The tissue surrounding a chronic cavity is fibrous, as a rule; sometimes the proliferating connective tissue of the wall shows a tendency to shrink and to pull on the adjacent tissue (fig. 197). Thus smaller cavities may be obliterated, or shrunken to a hollow space resembling a fistula.

In large apical cavities, the pleural adhesions usually prevent obliteration, but such rigid walls are not free of danger, for even after many years of complete healing, and disappearance of all tuberculous changes, some infection or other, *e.g.*, influenza, may initiate active secretion and necrotic decomposition within. Acute, diffuse, necrotic bronchopneumonia may cause death. Smooth lined cavities can often be positively differentiated from bronchiectasis only by the microscope (cf. p. 353).

Within older cavities (fig. 199), projections protrude like stumps; they consist of thickened remains of the supporting tissue with remnants of bronchi, and more frequently, of arteries, the walls of which have undergone changes until the layers are fused into hyalin connective tissue and the lumen more or less obliterated. Proximal to the occlusion, a thrombus is found, occasionally continuing to larger branches of the pulmonary artery. In other arteries, the lumen, surrounded by a thickened intima, is still recognizable. Not rarely, aneurysms are present (cf. p. 148), mostly single, rarely larger than a cherry, but not always easy to find during autopsy, since the softened wall, when ragged and torn, resembles a fibrin tag and may be covered with blood.

Arterial branches which show aneurysms are generally 1 to 3 mm. in diameter, occupying a small healed cavity which is filled almost completely. If the aneurysm ruptures, the hemorrhage (hemoptoe) may cause death by exsanguination; in moderate hemorrhages, the chief danger is suffocation due to the aspiration of blood (C. Gerhardt), which may also prove fatal in a short time. Less often, hemorrhage occurs from a vessel eroded by caseation and suppuration. Even if filling of the cavity with coagula ends the bleeding, it is usually repeated, since the tear cannot be closed by arteritis obliterans in a diseased vessel. The plugging of an aneurysm by

a thrombus, as in fig. 200, is favorable. In fatal hemoptysis, foamy, sanguinous masses are found in the bronchial branches, which often facilitates discovery of the source of hemorrhage. According to clinical data, hemoptysis occurs in 50% of cases of pulmonary tuberculosis. It probably hastens the course of phthisis by aspiration of blood contaminated by the contents of cavities (comp. C. Kaufmann). More details under hemoptysis, p. 378.

Quite large hemorrhages sometimes occur in the early stages of phthisis and in individuals apparently in the best of health, so they are often the first indication of trouble. These initial hemoptyses are supposed to be due to erosion of the smallest branches of the pulmonary artery, which, as direct neighbors of the bronchioles, are involved in the caseous disintegra-

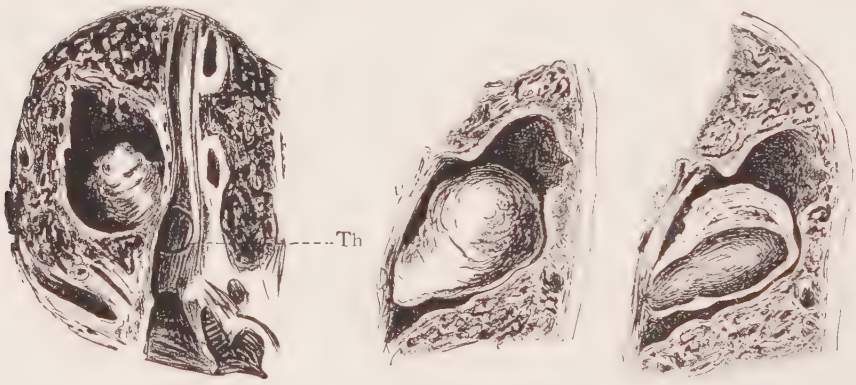



FIG. 200. FIG. 201. FIG. 202.

FIG. 200.—Aneurysm of the pulmonary artery in a phthisical cavity, filled by a thrombus (Th) which ends at the starting point of the aneurysm from the branch of the pulmonary artery, and shows a smooth, slightly concave surface; 53 year old phthisic; nat. size.

FIG. 201.—Aneurysm in a cavity of the right upper lobe.

FIG. 202.—The same on cross section, showing the aneurysm attached to a branch of the pulmonary artery. The aneurysm wall consists essentially of layers of thrombotic material. 46 year old woman; ⅝ nat. size.

tion, but they may also be due to erosion of veins in the wall of initial tuberculous bronchiectases (Birsh-Hirschfeld, comp. p. 349). Rare recurrent tracheal hemorrhages from venous distensions may be mistaken for pulmonary hemorrhages (comp. Freystadtl). In reference to rare cavernous carcinomas, see p. 471. Mycelia vegetation in cavities, on p. 480.

Relations of cavities to the pleura. The pleura is usually thickened above old cavities, and adhesions between the pleural surfaces are common, especially about the apices. In old cases, these adhesions seldom allow rupture of the cavity into the pleural space, but it occasionally occurs outward through newer pleural adhesions, or soft parts, or bone (sternum, ribs), (pulmonary fistula). The caseous foci which soften quickly, especially from mixed infections (fresh cavity), often rupture into the

pleural space; the cavity may be quite small, and is usually in the upper lobe; the perforation perhaps through a tiny opening is difficult to find.

Pneumothorax text on the cadaver. Lift the skin from the thorax and neck and pull upwards and laterally. Water is placed in the pocket thus formed, and covers the lateral and anterior section of the thorax; this is now punctured under the water and gas bubbles rise. Or the suspected pleural cavity is punctured and a flame (candle) is held to the puncture; if the tension is high, the candle may even be blown out. If the diaphragm bulges, pneumothorax can be demonstrated by filling the upper abdominal region with water and then puncturing the diaphragm. To directly visualize perforation of the lung, the suspected pleural cavity is filled with water, a catheter is introduced into the opened trachea, and air is blown in. If the pulmonary pleura is perforated, air bubbles rise in the water. This may also be done after removal of the lungs (including the organs of the neck) by immersing them in a vessel containing water.

Occasionally, one or more large openings are found in different lobes, or a thinned area is perforated like a sieve. The direct consequence of perforation is entrance of air into the pleural cavity, pneumothorax, but usually the result is a quick pyopneumothorax (comp. pleura).

A suppurative peribronchitis due to purulent disintegration of caseous foci may cause rupture through the pulmonary pleura before the advent of adhesive pleuritis.

(*b*) **Indurative Processes.**—Indurative changes appear at various stages and in most varying forms. Above (p. 424), the caseous-fibrous and the purely fibrous alteration of the tubercle have been mentioned. Even the first foci at the apex or elsewhere (near the pleura) may be encapsulated. The caseous contents may be thickened into a mortar-like mass after infiltration with lime; even bone formation is not rare (comp. p. 285). Such abortive forms of pulmonary tuberculosis are very frequent (comp. Konyevitz). In chronic phthisis, encapsulation of larger caseous masses occurs if they lie in tough, fleshy, or firm cicatricial tissue (fig. 197-d).

The chalky caseous masses cannot be removed with the knife, as can the calcification of bronchiectases (see p. 353). In time, the contained organisms die, although they often remain alive as long as traces of caseous material remain uncalcified, but may become so attenuated that they cease to be infectious. Perhaps after disappearance, spores may remain capable of development for a long time. They cannot be demonstrated by staining. Such a focus is considered healed only if animal inoculation (guinea pigs) is negative; a negative search for organisms is not sufficient (comp. Schmidt). Very frequently, small bronchopneumonic and peribronchial foci undergo a cellular fibrous change in their peripheries which starts from the surroundings and ends in complete healing, or at

least complete encapsulation. Thus are established a chronic nodular bronchopneumonia and chronic fibrous peribronchial tuberculosis or nodular and fibrous peribronchitis (figs. 196 and 198).

Frequently, the formation of tubercles and inflammatory cicatrization are combined, so that the oldest central portions of a focus undergo more or less complete cicatrization, while tubercle formation leading to caseation progresses at the periphery. In this manner, rosette-like figures with sunken centers are formed as hard, fibrous, gray, blue or black pigmented masses (black induration) while the periphery is studded with caseous, or caseous fibrous nodules of yellow or whitish yellow color. The black pigment is chiefly coal and only a small fraction is of hematogenous origin. Cicatricial fibrous changes are frequently seen in the apices (apical induration).

This indurating process, extensive enough to determine the character of the phthisis, in some cases is called "fibrous phthisis" or tuberculous pulmonary cirrhosis. Senile tuberculosis shows a tendency to cicatricial healing (comp. Hart), diffuse (fig. 197) or nodular or reticular (see below); the cicatricial mass, often slate gray, frequently contains a few light dots. The pleural surfaces are adherent and thickened.

The unaffected parts of the lung, especially alveoli between and around tuberculous foci, are secondarily changed by collapse on account of occlusion or compression of their bronchi. This may be accompanied by edema and hyperemia; the edema may age (p. 375) and appear glassy and speckled yellow, or splenization may predominate (p. 362). In other cases, the collapsed alveoli undergo atrophy without edema, the walls adhere (collapse induration) and develop into a pigmented cicatricial tissue (black or slaty induration). In still other cases, the alveoli are gradually compressed by the increasing inflammatory hyperplasia of interstitial tissue, and are obliterated in this way. Carnification occasionally extends over large areas (comp. p. 439), especially in encapsulation and partial cicatricial healing of small caseous foci (Ceelen). Not infrequently, complementary emphysema, accompanied by induration, develops around destroyed lung tissue, especially in chronic phthisis progressing by small foci. These lungs attain an extraordinary volume and the right heart becomes dilated. (In reference to bullous tuberculous emphysema depending on bronchial tuberculosis, see Orth.)

**Different Forms of Pulmonary Tuberculosis** (see p. 437).—The complicated picture of chronic tuberculosis of the lungs is composed of the anatomical details discussed in the preceding paragraphs; its character in individual cases is determined by the dominant process. At times, the further course follows the type already established in the initial foci, *e.g.*, a tuberculous bronchopneumonia marks the beginning and the disease

progresses by new bronchopneumonic lobular involvements to actual lobar extent, the most rapid form, leading possibly to the formation of cavities and ulcerative phthisis (galloping consumption). Chronic, caseous, confluent lobular pneumonias may appear coarsely nodular (caseous blocks, fig. 194). In other cases, peribronchial foci extending slowly dominate with cicatricial nodular healing. Again—and especially in the phthisis of advanced age—large portions of the lungs undergo cirrhotic changes (fibrous cirrhotic phthisis), combined, or not, with inclusions of

FIG. 203.—Very advanced pulmonary phthisis; cavernous cicatricial transformation of almost the whole, extremely reduced left lung. The cavities contained cloudy, dirty yellow thin fluid; walls show caseous deposits. Position of diaphragm at lower edge of IV rib. 36 year old woman. Slanting frontal section; $\frac{2}{3}$ nat. size (!).

encapsulated caseous blocks (see fig. 197) or with cavity formation, or bronchiectases. Frequently, the upper part of the lungs is occupied by very old, the lower part by more recent tuberculous changes. When more recent or older cavities are numerous, it is called "cavernous phthisis," which may be confined to one lung while the other is perfectly intact. In other cases, bronchiectatic, and sometimes also gangrenous phthisis develop.

There is no lack of attempts to classify this complicated chronic tuberculosis into its several types (Nicol, Aschoff, in opposition: Ribbert,

Beitzke), some of which also serve clinicians. Albrecht's classification into nodular, pneumonic, cirrhotic—with or without cavity formation,—has the advantage of simplicity, and according to Buttner, is also useful in x-ray examinations. It is not difficult to find these main types in the above chapter, but these are not the only ones. According to our opinion, it is practically impossible to devise a classification which includes all cases, because of the infinite variation of the process (see Schmincke, and the tabulation of A. Fraenkel and Graff, lit.).

Attempts toward better visualization of the variations are far more important than formal classifications, for then we can better understand the relation of development and extension from the condition of the organ, and the changes as they occur.

Ranke differentiates tuberculosis in man, especially the pulmonary, into:

I. *The Primary Stage.*—The (*a*) point of infection, and (*b*) related metastases by way of the lymphatics as far as the points of concentration, *i.e.*, the regional lymph nodes. *a* and *b* are designated the "primary complex." They are found especially in the pulmonary tuberculosis of children, but even in advanced old age although exceptionally. By contact increase (enlargement from within), *a* and *b* may spread. In its first stage, the primary effects are true exudative—later caseating pneumonic—but proliferative changes which often lead to healing, may dominate. II. In the *secondary stage*, two new factors enter the picture: (*a*) formation of hematogenous metastases in lymph nodes, bones, kidneys, etc., and (*b*) occasional acute exudative inflammations in the marginal portions of the foci already developed, *i.e.*, perifocal inflammation with the arrival of large numbers of lymphocytes frequently followed by caseation. Ruptures, which practically always occur, lead to the third form of metastasis, the intracanalicular (intrabronchial); contact growth, and these three avenues of metastasis (lymph—blood—bronchi) carry the disease to its climax (generalized tuberculosis). The various forms of reaction of the lung tissue, *i.e.*, proliferation toward the bacilli and exudation to the toxins, may be considered forms of histological allergy, or specific sensitivity to toxin, or oversensitivity, since allergy is a condition of changed reaction. Escape of toxic substances into the circulatory system, in analogy to the effect of tuberculin (comp. p. 426), must be held responsible for the spontaneous reactions of the exudative types. III. In the *tertiary stage* and its transition forms, the humoral metastases by the lymph and blood become less and less frequent, but contact growth and intrabronchial extension within the organ may continue undisturbed. There are cases in which the lung is gradually but completely destroyed after many years without distribution by blood and lymph channels, and in which not even

the regional lymph nodes undergo noteworthy changes (so-called isolated phthisis). In this stage, any organisms within the lymph nodes act merely as foreign bodies with the result of a humoral immunity or insensitivity to the toxin. As this develops, the general receptivity of the organs slowly decreases, but a predisposition of certain organs for hematogenous metastases is plainly seen, *e.g.*, the adrenals are occasionally involved alone. Tuberculosis may become stationary at any stage. Cases in which the disease passes through the three stages are in the minority compared to those in which the disease has once or several times been interrupted for longer or shorter periods. In an air-containing bronchial trunk, a new infection is always possible and the hematogenous route must not be ignored (see p. 437).

In these three stages, true primary, secondary and tertiary types must be differentiated. There are (*a*) true primary isolated pulmonary tuberculosis, (*b*) numerous secondary lesions from generalizing tuberculosis and (*c*) isolated pulmonary phthisis of the tertiary type, which is the chief typical chronic lesion. As stated, the course is frequently interrupted for a shorter or longer time; if the old process flares up (recurrent), or a new infection (usually aerogenous) is added, (pure infection), the disease then finds changed conditions as seen by the altered form of reaction (allergy), and it is this development of true isolated tertiary pulmonary phthisis with endobronchial extension but no lymph node involvement on a healed primary tuberculosis which is the most striking example (according to Ranke). In the petrifaction of a healed primary complex in the lung alongside of the true tertiary type, the immunization caused by the primary complex was sufficient to close the lymph and blood channels to the newly added disease. The secondary stage therefore does not appear.

Severe complications in the lung and pleura are seen in a limited number of cases. In reference to other changes in the pleura which is always involved in some manner, see the section, pleura. There must be mentioned: gangrene in cavities, gangrenous bronchitis, gangrene of the lungs, cavity hemorrhages, marked pleural exudate, pneumo- and pyopneumothorax, mixed infections, as with streptococci which may cause true septicemia, suppurative bronchitis and peribronchitis, extensive tuberculous bronchitis, general miliary tuberculosis.

We shall again briefly mention the various peculiarities of primary, mostly aerogenous (Albrecht, Ghon, Hart and others), pulmonary tuberculosis in children. The apices are not especially favored, (see p. 436). The paralytic thorax which causes such a predisposition is developed later.

A primary pulmonary focus is usually found, perhaps healed, but the process has almost always reached the lymph nodes (see p. 454). If the focus spreads, however, the picture of caseous pneumonia predomi-

nates, with the formation of large cavities, even in sucklings. Caseous pleuritis may also be present. Almost without exception, prompt extension into the lymphatic drainage of the lung is visible, *i.e.*, into the bronchial—and tracheobronchial lymph nodes (see bronchial and peritracheobronchial lymph nodes p. 259). They are mostly caseous, large, and hard or soft, but they may also be tuberculous without a single focus having formed in the lung (passage of bacilli through the lung). Rupture into the bronchi, see p. 428. Pneumonic processes, *e.g.*, after measles, create a predisposition. Compare Ghon and Roman (lit.) in reference to the lymphatic drainage of the lungs.

**Varying Severity of the Infection. Healing. Disposition.**—The development and course of pulmonary tuberculosis are essentially influenced by the number and virulence of the organisms which enter the lung, and by the resistance of the infected individual. It must be remembered that tubercle bacilli from the sputum of phthisics may be dried and whirled about with the dust to reach the lungs by inhalation. Cornet considers dried infected dust the most important source of infection, an opinion shared by Chaussé who considers such dust inhalation far more important than the spraying of droplets. Others (compare Kohlisch) consider this mode of infection as non-important. Chaussé found virulent bacilli in the dust of rooms inhabited by phthisics; further, according to him, dried bacilli retain their virulence for months. In the outside air no organisms could be demonstrated. Large masses of bacilli expectorated outdoors are destroyed by the sunlight or become attenuated. Virulent bacilli are found in the immediate proximity of the patient, and have been occasionally demonstrated on the utensils, clothing and books (Mitulesca) used by phthisics. They are also suspended in fine droplets of fluid sprayed from the mouth of phthisics while speaking, sneezing, coughing and are spread about their vicinity; Flugge's coughing droplet infection is quite dangerous for most humans. Infection from the alimentary tract, especially the glandular tuberculosis of children may occur from playing on the floor, but the relative danger is disputed (Bartel and Spieler, Ostermann, Beitzke). Probably unboiled milk may be a source of infection, although its share in the infection of sucklings is variously interpreted, high by v. Behring, less so by Flugge, Cornet, Heymann, (comp. B. Heymann, lit.), very low by R. Koch (see also references by Beitzke). Butter, cheese, etc., are less important. It seems curious that many more human beings do not die of phthisis, *i.e.*, about $\frac{1}{7}$ of all humans die from tuberculosis. Up to 1899, Germany showed an average annual mortality of 2.25 per 1000 inhabitants (Kohler). Since then in Prussia it has decreased, at least in adults (comp. Kirchner, B. Frankel, A. Gottstein and ref. by Beitzke). According to Kirchner, from 1876 to 1913 it

decreased about 55.8%, (comp. Orth); in Vienna in 1907 it caused 1/6 of all deaths (see D. 1908, 15, p. 661). If Schlesinger thinks that this diminution is due to a gradually increasing immunity, it is difficult to reconcile with the fact that during the world war with its hunger blockade, the mortality increased decidedly (Kirchner, Rubner and Fr. von Muller and others). In examining a total of 1992 cadavers, Naegeli in Zurich, and Burkhardt in Dresden, found tuberculosis up to 91%, Naegeli in adults even up to 97%. All these cases had been classified into fatal, non-fatal, latent active (chiefly caseation) and latent non-active (chiefly calcified foci). But Beitzke, like Kraemer, considers it unwise to generalize from these statements, since the data of Naegeli and Burckhardt apply only to hospital statistics from large cities rich in tuberculosis (comp. Stetter, Lubarsch). Many bacilli are probably arrested in the upper respiratory tract, especially the nose, and are expelled before they reach the lungs. Secondly, many individuals develop a sort of immunity against inspired bacilli, or, as it is expressed, have no predisposition, a factor, however, which, as emphasized by Flugge, is probably overvalued. In the third place, there is probably a difference in toxicity, *i.e.*, virulence, and, of course an influence due to numbers. Without a certain minimum quantity, say two to four hundred organisms absorbed, infection is not likely to occur (comp. Ziesche, lit.). Fourthly, healing of the tuberculous process often occurs during the first stages. Such curative processes occur especially in the apices where chalky foci embedded in scar tissue are often enough seen in strong individuals with never a suspicion of initial tuberculosis. This applies particularly to primary bronchial tuberculosis (comp. p. 349). But in ordinary tuberculosis of the lungs, under the influence of the natural protective forces, healing processes may also occur here and there (pp. 451 and 454), while in other places the tuberculosis slowly advances. Sometimes, even advanced cavernous phthises heal perfectly, perhaps leaving behind only a smooth walled cavity. But repeated pure infections are not rare, first, because complete immunization does not occur, and second, because humans are naturally predisposed to pulmonary tuberculous infection. Tuberculosis in advanced age is usually, although not without exception, more benign and harmless on account of a certain degree of acquired immunity (see p. 454). The cutaneous reaction of von Pirquet carried out with Koch's old tuberculin permits demonstration of infection in the living, and gives information of the extent of the disease (method, see Hillenberg); but its reliability has been doubted, for Hamburger considers with a negative Pirquet, that subsequent injections of large doses are necessary for diagnosis.

Sometimes the lung shows a local predisposition, *i.e.*, favored by anemia, stenosis, (see p. 94), while cyanosis (with left cardiac lesions) has

the opposite effect (see pp. 43 and 373). Dust inhalation diseases sometimes create a predisposition, as do various weakening diseases such as diabetes, undernutrition, pregnancy, possibly alcoholism—although according to others, in the latter condition, the opposite occurs (comp. Orth). This is called "acquired predisposition." Occasionally, trauma and tuberculosis are related, insofar as trauma favors an endogenous reinfection from an arrested focus, or stirs up an exacerbation in a chronic process (Orth). Descendants of phthisics are considered especially predisposed, *i.e.*, they possess hereditary individual predispositions sometimes recognizable in the so-called "habitus phthisicus" as peculiar changes in the form of the thorax developing during the years of growth (paralytic or asthenic thorax). It is viewed by Stiller as one of the symptoms of a congenital physical weakness, an asthenic constitution. The paralytic thorax is long, small and flat, the ribs droop, there are a long neck, long gracile limbs, muscular weakness, hypotonia, weak heart, splanchnoptosis, floating tenth rib, etc. The asthenic habitus predisposes to pulmonary tuberculosis (Hart), because the general space and circulation conditions of the apices (p. 435) are hampered, since the distance is greater from apex to hilum and the thorax is changed from its normal shape (Hedinger). The shortening of the first rib, by no means constant (mentioned, p. 435), is probably of no importance as a "mechanical factor" (comp. Bauer; other opinion by Hart). The inherited weak constitution is especially a detriment when such individuals are exposed to infection, *e.g.*, in close family relations.

Tuberculosis itself is not hereditary, at most only a predisposition, but tubercle bacilli may be transmitted to the germinal cells (germinal infection) or to the fetus (placental infection) and the child is born with congenital tuberculosis. v. Baumgarten calls this form of transmission "gennaeogenesis," but relatively few investigators join in the supposition that it is of greater importance than aero- or enterogenesis. Johne first demonstrated intrauterine transmission of tuberculosis in cattle (8 months old fetus); it has been seen repeatedly by others (lit. Takeya), and confirmed by experimental investigations, especially by Gartner, who succeeded in infecting some of the young by inoculating pregnant guinea pigs, white mice and rabbits. Bacillary transmission was successful even in the fertilized hen's egg (Muffucci, v. Baumgarten); the embryos developed and showed the disease after being hatched. Early tuberculosis in humans (v. Baumgarten, Veszpremi), the finding of tubercles and bacilli in the placenta and in the fetal liver, in cases of miliary tuberculosis during pregnancy, are responsible for the assumption that fetal infection does occur; apparently there is no doubt that it can be transmitted by the mother to the child (Pertik, Harbitz, Kaiser, Rollet, Dietrich, Ghon and

Roman, Dubois and others). But it is a great rarity and of little practical importance (Loffler, v. Behring, Schluter, lit. and others), except that the possibility should be admitted in some cases particularly of bones and joints (Kruse). But the assumption is rarely required if the opportunities of extrauterine infection, especially during childhood, are considered (Heubner). v. Behring thinks the first few weeks of life are the most dangerous period, and intestinal infection is the rule (Schlossmann also), while later infections are quite exceptional. Accordingly, the digestive tracts of the fetus and suckling perhaps lack protection, especially a mucous coating (mouth, stomach, ntestines) (Disse), but this anatomical supposition is incorrect because an unbroken mucous layer is present at an early fetal time (lit. in appendix). Experience, especially that gained from v. Pirquet's cutaneous reaction (p. 457) in the systematic examination of school children (*e.g.*, of Vienna by Hamburger and Monti), speaks loudly for childhood infection, at least in civilized countries and especially in big cities; but the opinion of Romer and others (see Schloss), that this concludes the infection, that adults can not acquire an aerogenous infection de novo and that the phthisis of adults is the direct result of the primary infection during childhood, is carried too far (see Hart, Selter, Beitzke). The infection need not be intestinal; indeed, Albrecht in Vienna on the basis of anatomical examinations of 1060 cadavers of tuberculous children found that the primary tuberculosis was in the lungs as a rule (1% primary enterogenous tuberculosis). Apart from the recognized greater susceptibility during childhood, "primary" tuberculosis may be acquired at any time during life and a new primary reinfection is certainly possible, even though the danger is diminished by increasing age. Reinfection, to which the lung is especially susceptible, is very important in the development of chronic pulmonary processes; it also shows that cure of a first infection does not confer complete immunity to the organism (comp. the various opinions of Roemer and Selter, Ranke). It is also a question whether childhood infection with bovine tuberculosis does not create a predisposition to later pulmonary phthisis (Orth). Consult the remarks on bovine tuberculosis and bovine tubercle bacilli under pleural and intestinal tuberculosis.

It has been emphasized that the pulmonary form is not necessarily a primary aerogenous infection of the lung itself, but may be secondary by way of the lymphatics (p. 434) or the blood from any other part of the body. It must be realized, however, that the passage of bacilli into the blood stream need not be acute nor in large numbers—this would produce general miliary tuberculosis—but a few bacilli may be carried, and if their number is not too small and they do not perish in the blood, which probably often occurs, they may settle in the lungs and produce a local infection.

Tubercle Bacilli in the Sputum. The number of tubercle bacilli in the sputum of consumptives varies greatly. Quick caseous disintegration allows small yellow clumps to appear in the sputum, which, for the greatest part, consist of the bacilli (p. 422, the granular form of tubercle bacilli). In other cases the bacilli are few in number and found only after repeated examinations. The antiformin method (von Uhlenhuth) is recommended; everything of the sputum is dissolved except the tubercle bacilli (more details by Schmorl). Negative findings do not exclude tuberculosis, positive findings are conclusive. In some cases the finding of bacilli is the sole evidence and neither pulmonary nor other symptoms point with certainty to the disease. X-ray examination is important. Elastic fibers have some diagnostic value. Animal inoculation should be done in doubtful cases (more details by Bartel).

**History of Tuberculosis.**—The importance of this theme justifies a short review of our knowledge of tuberculosis, but we must separate the anatomical-histological side from the experimental anatomical side. The term "tubercle" was used by the Englishman Baillie (1794), and the Frenchman, Bayle (1810). Bayle called the nodules which he found in numerous bodies dead of phthisis and consumption, tubercles. Laennec extended the conception "tubercle" to mean miliary nodules as well as caseous pneumonic foci, a uniform conception which has been favored by eminent investigators (p. 428 ff., etc.). A number of these, among whom are Langhans, Wagner, Schuppel, by careful study, have exactly described the histological character of a tubercle. Virchow upheld the idea of the duality of the process, contrasting the two forms of pulmonary phthisis, one characterized by the formation of nodules of a specific "miliary" character, and the other an inflammatory form leading to caseation. He believed caseation is not a specific process, but may also occur during the disintegration of cellular masses such as pus, tumors, etc.

The anatomical side of the question thus seemed to be settled. Then came the discovery, by the experimental method, that tuberculosis is an infectious disease with a specific virus, but the idea that it is infectious had already been expressed by Morgagni (1765), and sanitary precepts carried out by the police in the middle of the eighteenth century in some towns of France and Italy were based on this assumption. Klencke (1843) first reported transmission from man to rabbits; Villemin (1865) first proved that the subcutaneous inoculation of caseous pneumonic material into rabbits is capable of producing miliary tuberculosis of the internal organs. Villemin stimulated extensive research, which, however, led to much confusion at first. Many later investigations (Tappeiner and others) confirmed his results and proved that inoculation of rabbits with tuberculous material produced a nodular disease, the nodules correspond-

ing in their structure to human tubercles. Nevertheless, the nodules were not considered specific, since indifferent non-tuberculous material produced macroscopically similar nodules in rabbits (Lebert and Wyss and others). Thus Villemin's teaching, as not sufficiently proved, was pushed in the background, and the main object of demonstrating specificity of the nodules seemed to be forgotten. While many investigators, especially Klebs, emphasized and tried to prove the infectious nature of tuberculosis, it remained for Cohnheim to select the happy experiment of inoculation into the anterior chamber of the eye of rabbits. In this way he could follow the processes resulting from inoculation; when he used soiled material a general caseous inflammation, without general distribution followed, whereas, when he used tuberculous material, true tubercles appeared in the iris after an incubation period of one to several weeks (according to Baumgarten, in ten to fourteen days they are just visible macroscopically), later, in other organs (regional lymph nodes, lungs, liver, spleen, kidneys). Cohnheim (1879) thus proved conclusively that it is a transmissible infectious disease; it therefore followed that only such conditions could be classed with tuberculosis which could be successfully transmitted to a susceptible animal. Robert Koch in 1882, and Baumgarten independently, discovered peculiarly staining bacilli in pure cultures from human tuberculous material; these bacilli successfully transmitted tuberculosis to animals and were found in all tuberculous changes. They are therefore the cause of all true tuberculous processes. Baumgarten afterwards paralleled the bacteriological findings by exact anatomical investigations.

**Syphilis of the Lungs.**—Recent investigations have shown that syphilitic changes in the lungs of adults are fairly common, and are presented to the trained eye in a characteristic way. Elizade supplied the proof in about 30 cases by demonstrating the presence of the spirochetae pallida (Rossle). Lit. in the references of von Flockemann and Herxheimer, Milian in Cornil Ranvier IV 1912, French, Milne, Rosle and Elizade, numerous good illustrations. Clinically, it is diagnosed more often than pathologically (Kayser, Schroeder, Arnoldi).

There occur: (*a*) diffuse and nodular gummatous proliferations in the pulmonary connective tissue which, in contradistinction to tuberculosis, lead but rarely to disintegration and cavity formation (cavernous pulmonary syphilis M. Koch, Elizade), because, although they caseate quickly, they do not soften but are slowly absorbed leaving connective tissue and massive scars. To differentiate them from tuberculous scars, the absence of calcification (and caseation) is emphasized (v. Hansemann, Tanaka). Larger, tumor-like gummas to the size of a fist (histology and illustrations under muscles) appear, as a rule, in scars. They are soft

in the beginning and pale gray red; later they are firm, homogeneous and white yellow. According to Elizade, their favorite sites are the vessel and bronchial walls. They soften and ulcerate (rupture into bronchi), or undergo fibroma-like sclerosis. To differentiate them from tuberculous caseous foci, apart from the finding of bacilli (animal inoculation), it might be pointed out that gummata are always more firm than tubercles, usually lie in sclerotic tissue, always have a connective tissue capsule (Virchow), have few giant cells, are mostly in the middle lobe, and practically never in the apex. (*b*) The more frequent form, occasionally combined with gummas, is the interstitial syphilitic pneumonia, the early stage of which is characterized by intensive proliferation of the cells of the alveolar walls in the vicinity of small bronchi, arteries, interlobular septa, etc., (acute interstitial pneumonia); miliary gummas are scattered here and there in this tissue (illustr. by Roessle). It has a peculiar gelatinous appearance; Stanley and Elizade speak of the first or catarrhal stage with beginning inflammatory new growth. Later, more and more connective tissue is developed provided that no more gummas are formed from intensive action of the spirochetae (indurative pulmonary syphilis, Orth; sclerotic syphilis, Mauriac, Elizade and others). Thus there are large, irregular, net-like or chess board-like, white cicatricial strands which sometimes follow the bronchi, arteries and interlobular septa, and scars extending to the thickened and adherent pleura and retracting the lung surfaces (pulmo lobatus) or spreading like rays from the hilus into the lung tissue. In between are air-containing, or emphysematous, or atelectatic areas of lung tissue. Less commonly the sclerosis is dense and the lungs are shrunken and contracted; the section surface is iron gray, dense, and interspersed with rounded emphysematous areas. These thickenings are often extremely firm and cicatricial and may contain an abundance of elastic fibers (Stanley) and newly formed smooth muscle (Tanaka, and comp. p. 399). The cicatricial masses, however, have no specific histological characteristics. The lower lobes are most frequently involved. (*c*) Nodular hardening occurs around the smaller bronchi as in pneumoconiosis, but usually confines itself to circumscribed areas. Tubercle-like nodules suggest an obliterating gummatous bronchitis (Schmorl). It has been pointed out that simple catarrhal bronchopneumonias develop under the influence of syphilis, and disappear after antisyphilitic medication.

Congenital pulmonary syphilis occurs in the newborn and even in fetuses of later months (after the 5th); it is very frequent; Thomsen found it in 80% of syphilitic fetuses over 6 months old. Syphilitic changes occurred in the pancreas in 87%, liver 83%, spleen 74%, bones 97%.

The changes are varied. There are differentiated: (1) circumscribed gummas, as rounded, pale, gray red, glassy nodules with sulphur yellow

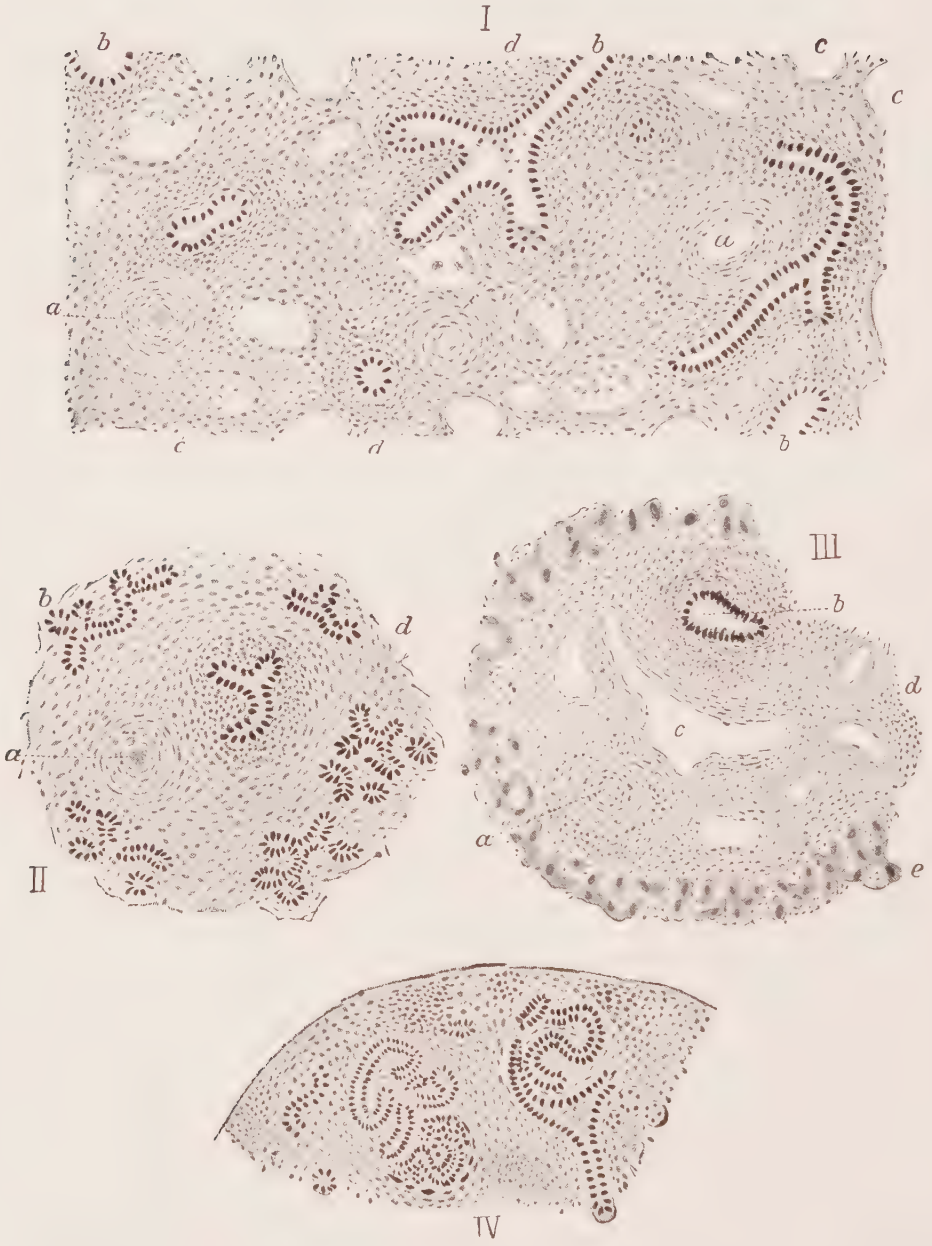
inclusions, slightly prominent, if superficial (fig. 208). This form is relatively rare. (2) Pneumonic processes are mostly diffuse, far more common, and often exclusively (*a*) interstitial. This form is practically characteristic of syphilis; but others are (*b*) alveolo-catarrhal, characterized by fatty degenerated epithelium with admixture of leucocytes; as a rule (*b*) combines with (*a*).

It is doubtful if (*b*) ever occurs alone, but the alveolar changes may predominate in rare cases when the alveoli contain large numbers of leucocytes and desquamated epithelial cells undergoing fatty degeneration. The color of the airless lung is white to gray white and it has a firm leathery consistency. Virchow's designation "hepatization or white pneumonia" is applicable only to such cases. The pure form without interstitial changes is doubtless very rare (Kokawa). The color is not decisive because bluish red, hepatized lungs with complete absence of white are also seen in macerated fetuses.

**Microscopical.**—Slight interstitial and alveolar changes cannot be recognized macroscopically, but smears made from the lungs of stillborn infants, or from those which lived for a short time, show fatty degenerated alveolar epithelium and leucocytes with extraordinary frequency. But care is advisable in diagnosing syphilis, since the stillborn, especially premature, normally show abundant fat droplets in the alveolar epithelium (Aschoff). For this reason a cut and stained section should be examined for the deciding interstitial changes (demonstrate spirochetae!), sometimes under the dominance of small cell infiltration, but characteristically with marked thickening of the interstitial tissue whether perivascular and peribronchial or interlobular or interalveolar. There is a great abundance of spindle or polygonal cells (fibroblasts) or of fibrous, connective tissue more or less rich in spindle cells (older changes). The latter is deposited mainly in blood vessels and the fibrous thickening of even small arteries is striking (*a* in fig. 204). The alveoli react variously; if the interstitial proliferation is marked, frequently neither alveoli nor bronchi are developed, merely branching channels here and there and acinar clusters lined with cuboidal or cylindrical epithelium, are reminiscent of the early fetal lung (Stroebe).

Doubtless this arrested development is caused by the syphilis, just as in the kidneys, etc. (lit. by Kimla). Woenkhaus recently described unilateral fibrous pulmonary atrophy in a 15 year old girl with congenital syphilis and demonstrated abortive bronchioles and absence of alveoli, from congenital lack of development of lung tissue. The growth of elastic fibers is also disturbed, being delayed or completely inhibited (Kokawa).

The lung may contain little or no air, but may gain in volume, become fleshy, tough, difficult to tear, and on section appear uniformly smooth, glassy, gray white, white red to white.




FIGS. 204 to 207.—Various organs in congenital syphilis. Child 40 cm. long, died soon after birth. I. Lung. A, arteries markedly thickened; b, bronchi, gland-like; c, alveoli, sparse, with partly desquamated epithelium and some round cells; d, cellular proliferating stroma; granulation foci with abundance of round cells especially around bronchi. II. Pancreas. a, markedly thickened artery; b, glands; in the center of the picture an excretory duct; d, similar to I; cellular infiltrate around the duct. III. Liver. Artery as in I and II; b, biliary duct; c, portal vein, walls infiltrated; d, as in I, granulation foci rich in round cells especially around a and b; e, liver cell columns. IV. Kidney. Cellular proliferating stroma containing foci rich in round cells and urinary tubules and glomeruli in developmental stages.—(I to IV medium magn.).

Sometimes there are spots of cloudy yellow color and loose structure (alveolar pneumonic areas) or spots of denser, lardaceous, compact structure (gummatous areas).

There are transitions from the diffuse forms to nodular gummatous proliferations, the latter representing merely more local cellular proliferations with a tendency to caseation and cicatricial metamorphosis.

The term "white pneumonia" has been applied to the diffuse interstitial pneumonia of gray white color, but this leads to confusion with the "white hepatization" of Virchow. The latter term is reserved for the rare cases described, and we speak of interstitial or syphilitic pneumonia, or in suitable cases, of white carnification. [For discussion of

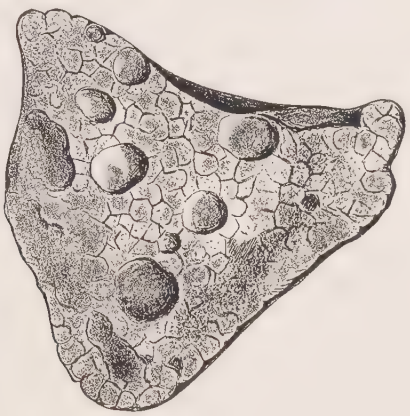


FIG. 208.—Lower lobe r. Lung with gummas bulging on the surface as more resistant lighter areas; spirochetae were found; child 2 months old; 5/6 nat. size.

syphilis of the lungs, see Rulsstinat G. J. Arch. Path and Lab. Med. 2: 473: 1926.—*Translator.*]

**Glanders of the Lungs.**—(Consult under nose, p. 298.) Glanders frequently attacks the lungs via (*a*) the air route, and probably more frequently, (*b*) the blood stream. The results vary. Cellular nodules resemble tubercles because of frequent central caseation (for differentiation, see p. 299). Sometimes the nodules have red coronas; in other cases they are purulent and almost fluid, in fact, true abscesses; in still others, there are lobular, or even lobar pneumonic, white, dry, or caseous, grumous infiltrations resembling caseous pneumonia, or again, septic infarcts with hemorrhagic borders often undergoing purulent liquefaction and abscess formation (glanders cavities). Metastatic abscesses, resembling pyemic abscesses, are rounded and often present in large numbers to the size of cherries and larger, favoring the lower lobes (histology by McCallum, Zieler).

Glanders of the lung has no macroscopical characteristic changes and is easily mistaken for caseous pneumonia.

**Actinomycosis of the Lungs (and Pleura).** (Lit. in Appendix.)—The disease is relatively rare. The actinomyces or ray-fungi enter the lung by the air route, on grains, beard, fragments of a carious tooth (J. Israel), etc., or indirectly by immigration from the esophagus (Ponfick, Soltmann, v. Baracz, lit.).

Metastatic pulmonary actinomycosis, *e.g.*, from intestinal actinomycosis (Benda), is rare.

The mouth is the most frequent portal of entry and localization of actinomycosis. Other portals are the intestines, lungs, very rarely an external lesion. Actinomycosis may actively invade every organ by continuity or via the blood and lymph channels.

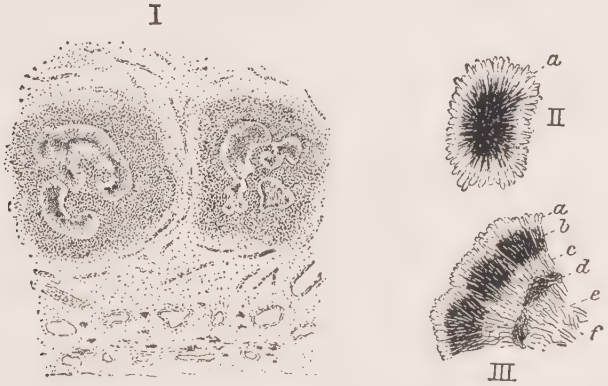
**General Effect of Invasion of Actinomyces. Morphology.**—The tissues react to the actinomyces by producing nodules of granulation tissue rich in vessels, leucocytes, lymphoid and epithelioid cells, some giant cells, perhaps many (Rossi), and eosinophiles, although relatively few. This tissue is tumor (sarcoma)-like with large cells, and in some organs such as the heart, kidneys, especially the liver, produces nodules the size of an apple or larger. Fungus colonies occupy the centers of the cellular foci (fig. 209). The vascular granulation tissue surrounding the colonies may undergo further changes in two directions, (*a*) softening, and puriform solution, for typically it has a tendency to fatty or lipoid degeneration. This produces actinomycotic abscesses, or cavities or pus channels, filled with soft friable masses containing fungi and surrounded either by cellular (younger) granulation tissue which is sulphur yellow from the so-called pseudoxanthoma cells rich in lipoids or by older tissue, cicatricial and hard (fig. 209). Microscopic examination shows pus or fatty debris, granular cells, nuclear fragments, isolated red blood cells, sometimes mucoid metamorphosis. (*b*) The nodules harden, undergo fibrous change and contract, until the process is walled off or actually healed. The pictures especially characteristic of actinomycosis (fleshy scar tissue penetrated by granulation foci which shows fatty degeneration, friable or purulent cavities and fistulae) are actually produced by a combination of (*a*) and (*b*), *i.e.*, by softening (suppuration and fatty degeneration) and fibrous metamorphosis. Harbitz and Grondahl term actinomycosis a chronic suppurative inflammation with reactive granulation tissue.

The most important structures are, however, the fungus colonies. The similarity of the radially arranged colonies to some crystal complexes has led to the term "ray fungus." Tubercle bacilli may show similar forms in the animal body (Schulze, Lubarsch, Friedrich and Nosske) and occasionally bacillus fusiformis also, in which the clinical (pyemia), ana-

tomical and histological pictures may resemble actinomycosis (Coronini and Priesel, lit.).

The fungi are minute, or macroscopically visible bodies reaching the size of poppy seeds and of yellow, gray, green or brown color. After death of the fungi, calcification of the colonies sets in, and the granules are easily isolated by washing away the softened masses with the pus as sediment.

Microscopic Demonstration. Light pressure on the cover glass (examination in water, glycerin or dilute acetic acid) breaks the granules into gland-like colonies, gray yellow in the unstained preparation (low power) and containing the clubbed thready fungi. The unstained actinomyces




FIGS. 209 to 211.—Actinomycosis of the pleura. I. Actinomyces—colonies, some kidney-shaped, embedded in dense masses of leucocytes, surrounded by vascular cicatricial connective tissue; radiating clubbed forms in the peripheral lighter areas of the colonies cannot be seen with this magnification. Carmine stain; (low power). II. Actinomyces colony with broad red ray envelope (a) within, central violet threads, some radiating out into the clubbed layer (stained rose-red) stain see below. III. Piece of a fully developed colony; a, clubbed border; b, richly branched; c, slightly branched; d, germinal layer; e, root plexus; f, centre of colony. Designations according to Bostroem. II and III stained with anilin gentian violet and eosin; (high power).

unit has a granular or radially striated design, and often a zone of light pear-shaped bulbs or clubs at the periphery. The granules give the iron reaction (p. 372). By suitably staining a smear, or better, cutting a section of tissue (10% solution formalin, celloidin preparation, hemalum-eosin, or Gram stain) the classic picture of a perfect fungus appears, *i.e.*, a finely granular center from which the threads radiate (fig. 210); clubbed ends are Gram negative, but stain quite sharply with eosin, fuchsin, etc., as counterstains, although hemalum-eosin preparations differentiate well. The early forms are networks of fine and twisted threads, either starting from one point or completely felted together. In very early cases the fungi are absent in the pus (comp. Dressel). Johne and Ponfick first successfully transmitted actinomycosis to animals. O. Israel and Bostroem have grown pure cultures; those on agar are of peculiarly gland-

like radiating structure. Wolff and J. Israel succeeded in inoculating pure cultures into animals (abdominal cavity of rabbits and guinea pigs). Bostroem has described the structure and development of the fungi; according to him, the actinomyces are branching hyphomyces, their branches are solid tubes, which, on continuous transverse division, gradually break into rounded spores, (Gasperini shares this opinion, which is contradicted by Wright). The clubbed distal swellings of the otherwise uniform tubes are due to a regressive change, a gelatinous swelling of the thread capsules. The spores may develop into threads and thus form new colonies. According to Bostroem, a fully developed colony is a hollow hemisphere from the open side of which mycelial threads and network grow out and invade the vicinity, and this takes place in such areas where the radial arrangement of the mycelium is interrupted (see fig. 211) (Loele).

Much uncertainty prevails as to the position of actinomyces in the botanical system. Kruse classes them with the streptotrichiae which structurally resemble hyphomyces, but, on the other hand, if the slightly twisted branching threads become fragmented, they resemble bacteria, and with leptothrix and cladothrix, belong to the trychomycetes, which are a special group in addition to fission—mold—and budding fungi; they are, therefore, morphologically and biologically between mold and fission fungi. See section IX in reference to streptothrix infection.

The fungus remains viable in dried grain for more than a year (Schlegel, lit.). According to Berestneff, there are more than 40 species of the genus actinomyces which can be cultivated from hay, grain and straw; others believe that not these aerobes, but only a single anaerobe is the true actinomyces hominis (Wolff-Israel, Wright, lit., Shiota, Harbitz and Grondahl, Dressel). According to Wright, this anaerobe exists normally in the secretions of the buccal cavity and in the gastrointestinal tract in the form of fragmented filaments. Dressel states that there are diseases clinically and anatomically similar to actinomycosis, in which the gland-like structures, found in the pus, consist of aerobic streptothrix types (actinomyces group, Bostroem). (See Melchior in reference to fuso-spirillosis of the neck, resembling actinomycosis before the beginning of the fistulous stage.)

Actinomycosis of the lung begins in the bronchial mucosa, or in bronchopneumonic or peribronchial foci. The diseased areas are characterized by the granulation masses and actinomyces above described. Larger nodules and nodes are surrounded by connective tissue in which softening cavities develop and eventually perforate the bronchi (organisms in sputum) or, more frequently, a massive cicatricial connective tissue growth at once surrounds the granulations and extends from the lung to the pleura causing obliteration of the pleural cavity.

In the firm cicatricial tissue occupying larger areas of the lung, the granulation tissue masses are preserved in the form of branching fistulous tracts and foci filled with pus undergoing fatty or mucinous degeneration. The quantity of the latter is remakably small; the color is yellow, often hemorrhagic; it contains the fungi.

H. Merkel described a tumor-like actinomycotic proliferation the size of a fist, between scars, which was remarkable for the large quantities of doubly refracting substance it contained.

Usually the lower lobes are affected, but apical infection also occurs (the author; Shiota).

Sometimes the further course is exceedingly complicated. By continuity the process extends to the tissues of the neck and produces immense, lateral, cicatricial, fistulous masses in which the large vessels are embedded; it then proceeds as a prevertebral chronic phlegmon to the spinal column and may ascend or descend. But the invasion may, ignoring every anatomical boundary, enter adjacent cavities and organs such as the mediastinum, pericardium, heart and become a general disseminating actinomycosis, (see p. 17), in peritoneum, liver, spleen, but the most marked characteristic is passage through the intercostal spaces and appearance on the outer aspect of the thorax. Extensive cicatricial thickenings develop in the musculature, subcutaneous tissue and in the skin with innumerable fox burrow-like fistulous tracts. These characteristic chronic phlegmons with fistulous suppuration occur everywhere over the whole back and spread to the ribs and the spinal column. It may even re-invade the thorax (J. Israel). By continuity along vessels and nerves, it reaches the cranial cavity (meninges and brain), but involvement of these organs is more often due to hematogenous metastasis. Clinically the picture of a chronic septic pyemia is developed or the cachexia is fatal; it is not rarely accompanied by amyloidosis.

The pleura may be involved by another route, namely, a primary focus in the mouth (p. 558), granulations and fistulous tracts along the spine to the ribs, the vicinity of the pleura (peripleuritis).

Actinomycosis is not rare among cattle and pigs.

### Tumors of the Bronchi and Lungs (Lit. in Appendix)

**Primary Tumors.**—Benign tumors, such as adenomas, spring from the bronchial mucous glands (Chiari); according to some, they may be congenital and more complex (Leuba), causing massive bronchiectasis; small globular lipomas, pedunculated fibromas (Knack, Pfeiffer), papillomas or papillary fibroepitheliomas, multiple primary myomas (Deussing) of the bronchi are rare. Chondromas, usually solitary, size of a pea to walnut, rounded and nodular, are but rarely true ecchondroses (Siegert); most of

them have no relationship to the bronchial cartilage (displaced cartilage anlage?) but are located in the lung tissue or below the pleura where they project or may be plucked off from the surface. They sometimes consist of reticulated cartilage, and may partially ossify. Rounded, nodular, or coral-reef-like pronged osteomas are rare, at most the size of a cherry. Not to be classed with tumors are the very frequent, usually small, irregular, occasionally branching bone formations, developing metaplastically from connective tissue, etc., also found around calcified caseous nodules, as described by Lubarsch and Pollack, Ratinska, Schlagenhaufer, Simmonds, Nelius and others. Among malignant tumors, sarcomas of spindle, round (Eckersdorff, lit.) and mixed cell types with giant cells (Glass) are very rare; usually they are voluminous growths which occupy a lobe or even the whole lung. It is difficult to recognize their starting point, *i.e.*, lung or pleura. In some of these rare cases, the diagnosis was made by examination of the sputum (Bocage, Guyot and Parcelier, lit., Bernard). There also occur stenosing intrabronchial pedunculated sarcomas with subsequent bronchiectasis, the so-called "cork sarcomas" (Braxton Hicks and lit. by Kirch). Hebbing, Zipkin have each described a teratoid (adenorhabdomyoma), and Katase a teratoma.

Carcinomas are moderately rare. According to the material at Basle, they constitute 1.76% of all carcinomas; according to that at Breslau 1.83% (Passler); the majority are bronchial, the minority pulmonary (epithelium) in origin. Men between 40 and 60 years of age are most frequently the victims, although the author saw bronchial carcinoma in a man 30 years old. The right lung has a remarkable predilection.

The following data are compiled from large statistics. According to our own relatively small numbers, 24 cases in Basle (left columns of table), 22 cases in Gottingen (right columns), women are in the majority, which is exceptional. The oldest woman was 83 years of age, a rare finding, since advanced age is usually not attacked (comp. Eppinger, lit.). See also numbers by Briese (youngest case, 26 years old; oldest, 84 years; 44 men, 16 women).

| Age | Men | Women | Total | Men | Women | Total |
|---|---|---|---|---|---|---|
| 30–39 | 1 | .. | 1 | 3 | 1 | 4 |
| 40–49 | 2 | .. | 2 | 4 | .. | 4 |
| 50–59 | 3 | 3 | 6 | 8 | .. | 8 |
| 60–69 | 4 | 5 | 9 | 4 | 2 | 6 |
| 70–79 | 1 | 4 | 5 | .. | .. | .. |
| 80–89 | .. | 1 | 1 | .. | .. | .. |
| | 11 | 13 | 24 | 19 | 3 | 22 |

As Langhans has shown, most of them originate from the bronchial mucous glands, but some are derived from alveolar epithelium. The cells are frequently large, rarely long, cylindrical, or ciliated (Horn); indeed they are extremely variable in shape, often rich in nuclei, in a few cases they are smaller, low cylindrical or cuboidal resembling both alveolar epithelium and mucous gland cells; they are not easily differentiated from those of a round cell sarcoma. Sometimes there are hollow strands with one or more layers of cells, at times containing mucus (adenocarcinoma); but in the same visual field may be seen solid cell masses jumbled up with the gland imitations. The author saw thick mucous droplets in the cells and microscopically and macroscopically the typical picture of mucoid adenocarcinoma. In the 83 year old woman mentioned above (fig. 213) an adenocarcinoma derived from the bronchial mucous glands lined many pulmonary alveoli with one layer of cylindrical cells, as in primary carcinoma of the lung (p. 473) or the more frequent metastatic carcinomas. The alveoli were filled with mucus, while in other places the carcinoma infiltrated the interstitial tissue and the septa with the characteristic structures of adenocarcinoma (microscop. illust. by Boecker). In other cases, the tumor is a squamous cell carcinoma (Orth, Doemeny and Watsuji) with laminated spheres and cornification originating from flat alveolar epithelium or metaplastic bronchial epithelium. In the lower lobe of the right lung of a 46 year old man, the author saw a ragged cavity the size of a fist, its wall consisting of tumor masses composed of cornified and calcified pavement epithelium. Squamous cell carcinoma (very rarely cylindrical cell carcinoma, see lit.) has originated in the walls of bronchiectases and old phthisical cavities, (rare), (Friedlander, Wolf, Schwalbe, v. Hansemann, Perrone, lit. and others). Such cases can be easily overlooked during autopsy. Ernst described a squamous cell carcinoma of a bronchus.

Some of the so-called "pulmonary carcinomas of Schneeberg," found frequently in workers in the cobalt mines near Schneeberg, proved to be lymphosarcomas (E. Wagner and lit. by Uhlig). Arnstein found a non-cornifying carcinoma metastasize, as a round cell squamous cell carcinoma. It might be thought that the dusty lung is perhaps predisposed to carcinoma as in anthracosis and chalicosis (comp. Schmorl by Uhlig). Round cell sarcomas have also been observed.

Macroscopically there are several forms:

1. Bronchial wall tumors near the hilum appear as (*a*) soft, nodular, sometimes papillary growths (1) more or less obstructing the lumen, or (2) as circumscribed stenosing infiltrations confined to one area, practically never in the main bronchus, but usually in a bronchus of the first or second division, or as (*b*) a growth spreading in its circumference with the bronchus in the center, or (*c*) as a tumor starting at once from the hilum and

extending by retrograde transport by way of the lymphatics in thick stringy infiltrates and sclerosing sheaths into and around the bronchial walls and vessels and from here into the lung; or (*d*) starting at once from near the hilum and invading the larger and smaller lymph channels as far as the alveoli, in retrograde direction as a so-called carcinomatous lymphangitis of the lung and finally of the pleura. Isolated nodules may be situated in other lobes.

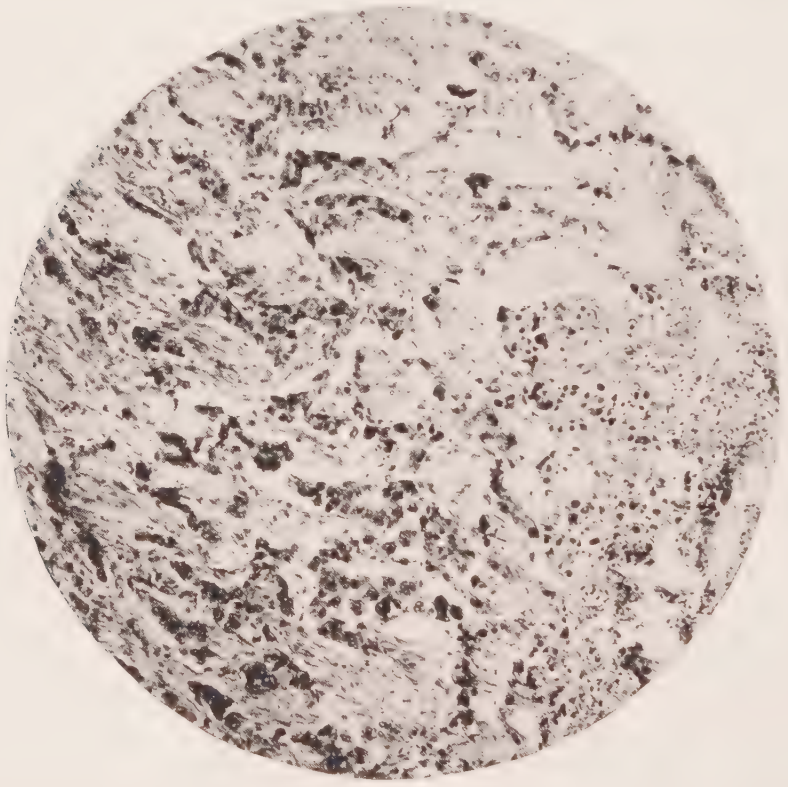


FIG. 212.—Primary carcinoma of the lung. Large cell type producing in some areas, gland-like formations. This was present in a man 37 years old whose first complaints were shortness of breath and whose first physical signs led to the diagnosis of pleurisy with effusion. The nature of the pleurisy was soon manifest on removal of the fluid, for it was bloody and contained numerous cells obviously not inflammatory but neoplastic. The origin of this growth was about in the middle of the right lung from which it spread as a large nodule from which smaller strands radiated in all directions. The pleura was coated over an area about as large as a saucer with a thick layer of tumor cells. × 110 L. H.

In (*a*) there is an annular thickening of the bronchial wall, nodular swelling, and ofttimes ulceration of the mucosa. The lumen is narrowed, and the dilated bronchi behind are filled with glassy mucus, muco—pus or putrid masses. The tumor may be white or yellow white, gelatinous, transparent, hard or poultaceous and soft. It is often small and is occasionally overlooked especially if situated exactly where the bronchus is cut

as each lung is removed separately at autopsy. The author recommends removal of the lungs in toto, including the organs of the neck.

(*b*) Strands from the primary nodule follow the lymphatics as far as the pleura which contains nodules and diffuse infiltrations.

(*c*) The infiltration is very dense and completely displaces the lung tissue. The pleura may be infiltrated to the thickness of a finger and react by an exudative pleuritis of sero-fibrinous, hemorrhagic character.

(*d*) The lymph channels within the lungs become delicate tumor strands with small nodules along their course, and the pleural lymph vessels appear like rosaries.

(*2*) The diffusely infiltrating forms reach the size of a baby's to a man's fist; indeed a whole lobe may be replaced by gray, gray red, glassy foci which yield mucinous masses on scraping or appear like caseous pneumonic foci as the expression of the multicentric extension. The bronchi and large lymph vessels of the interstitial tissue may escape. This form includes:

(*a*) True carcinoma of the lung with cylindrical to cuboidal epithelium, papillomatous architecture and gelatinous degeneration. The pulmonary alveoli are the stroma of the tumor (it is termed "alveolar carcinoma"); or (*b*) one which starts from a bronchus which is a sort of stem to the infiltrated area.

If it arises at the bifurcation, it may extend almost symmetrically into both lungs. Briese (lit.) described a case in which both lungs, enlarged and very heavy, were filled with a mucoid papillary adenocarcinoma but the bronchi and interstitial tissue remained free. Only the hilum and prevertebral lymph nodes were infiltrated.

**Circumscribed tumors** in the middle of a lobe may be soft or hard, more or less rounded and of various sizes. Nodular dissemination occurs in the vicinity and finally into the other lobes of both sides. The starting point is the lung itself, or probably more often, a bronchus; recognition is based on the microscopic findings (fig. 213).

There are combinations of these types.

In *2* and *3* the tumor replaces lung tissue and penetrates the alveoli which are filled or lined with its cells while the epithelium is destroyed. The cells also penetrate the pores from alveolus to alveolus. (The same process is observed in metastatic nodules,—Treutlein.) The infiltrations and nodules may resemble bronchopneumonic, or caseous foci, especially when tuberculosis is also present. Disintegration into cavities which may communicate with a large bronchus is common. Not infrequently, hemorrhages or gangrene occur in the cavities. Clinically, the picture may resemble disintegrating caseous tuberculosis (Grau), but the diagnosis may be made by finding tumor cell groups in the sputum. Lenhartz considers fat granules and globules in the sputum especially characteristic.

The pleura is seldom spared and the exudate is often hemorrhagic. Rare cases occur without local symptoms, and the metastases in other organs (*e.g.*, in the brain, see p. 475) so dominate the clinical picture that the diagnosis is led in the wrong direction.

Consult Hampeln for symptomatology (lit.), Otten for x-ray diagnosis.

The subsequent events vary according to the type and extent of the growth. Infiltrating forms, even if very small, cause stenoses, frequently

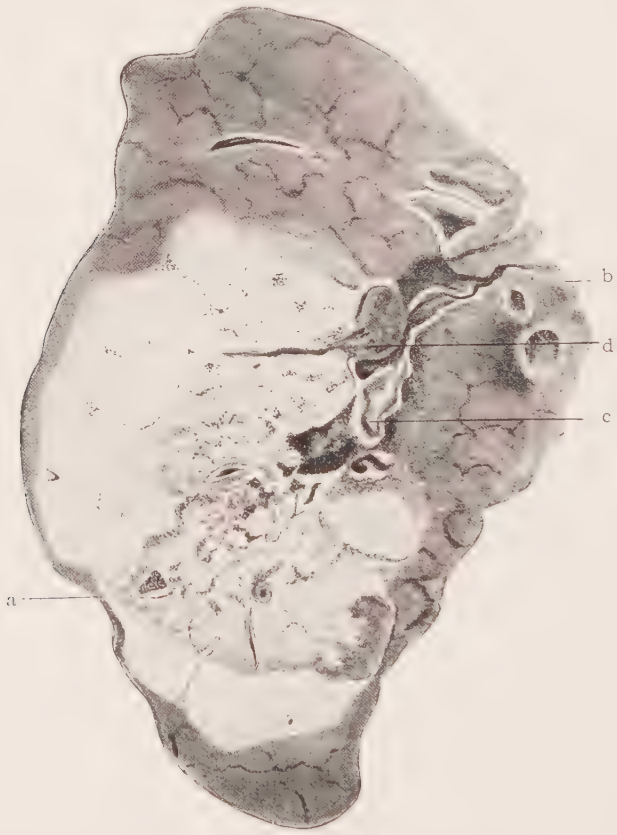



FIG. 213.—Adenocarcinoma in l. lower lobe (pulm. anthracosis). Frontal section of case mentioned, p. 471, woman of 83. a, thickened pleura; b, direction of hilum; c, bronchus; d, branch of pulmonary artery with thrombus. Nat. size. (Consult E. Boecker, V.A. 202, 1910).

with consecutive bronchiectases. The bronchi contain pus, muco-purulent, or putrid secretions, or, more often, tough, spirally twisted masses of mucus. The author autopsied such a case complicated by asthma (published by A. Schmidt). Smaller hemorrhages (raspberry jelly sputum in tumors of the lung, Stokes) are relatively frequent, and important in the diagnosis (A. Frankel). Massive hemorrhages are rare, but occur from disintegration of soft infiltrations and nodules, or from small

bronchial ulcerations. In a 52 year old man with carcinoma of the right bronchus, a small bronchial ulcer eroded the right branch of the pulmonary artery; the hemorrhage suffocated the patient; the same condition was observed by the author in a 61 year old man; tumor in the right bronchus first bifurcation; in another case (man 75 years old), a carcinoma in the main bronchus of the right lower lobe caused fatal erosion of the pulmonary vein. Schmittmann saw rupture into the heart. Disintegration may cause aspiration pneumonia and gangrene of the lung. Marked involvement of the pleura by carcinomatous cicatrices, nodules and circumscribed plaques in combination with exudative pleuritis may compress the lung and mask the true ailment. Metastases are frequent in the bronchial lymph nodes, sometimes as secondary growths; they may cause severe broncho-stenosis. At times, the metastases appear in the other lobes of both lungs. Both the mediastinal and supraclavicular nodes may be involved, but occasionally the growth spreads to many internal organs, especially the liver. In a 40 year old man with a small bronchial carcinoma of the left lower lobe, the author saw a carcinomatous liver weighing 4700 gms. The bones are also subject to metastases, especially the spine which may collapse. In a case at Breslau, 63 year old man, bronchial carcinoma in left lower lobe, clinical diagnosis: right hemiplegia, the author saw a small mucoid carcinoma of the bronchus and innumerable cystic metastases in the brain; in another case with a small bronchial carcinoma, metastasis occurred in one adrenal gland and in the brain. The author saw a 47 year old woman with carcinoma of the left lower lobe and multiple metastases in the brain in whom the lung tumor was unrecognized, the clinical diagnosis being primary brain tumor, for which she was operated, (more details under brain). Sometimes extension to adjacent organs takes place by continuity, but rarely over large areas. In a man 32 years of age, the author saw a bronchial carcinoma (round cell), the size of a hen's egg, coming from the hilum and causing stenosis; massive lymph nodes were filled with soft, voluminous, nodular tumor masses which displaced the heart to the left (carcinomatous fibrino-hemorrhagic pericarditis) and ruptured into both auricles (especially the right) as smooth, white, bulging, soft, finely villous extensions; the esophagus also was infiltrated; metastases were found in both adrenals, a small one in one kidney, two nodules in the pancreas, a tumor as large as an apple in the interior of the right hepatic lobe; the clinical aspect was that of a mediastinal tumor.

**Secondary Tumors.**—Metastases are especially frequent in the lung in the form of (*a*) nodules, usually multiple, of varying size, submiliary, miliary (in great numbers) to the size of a fist and more, and often near the periphery, occasionally almost projecting as though merely fixed to the pleura.

They are chiefly the various sarcomas and carcinomas (fig. 214); in the latter (from the stomach, etc.) perhaps many minute hematogenous metastases are found only microscopically (p. 480). Chondromas are rarer as plugs within vessels (Ernst) or as true nodular metastases. Melanotic and round cell sarcomas are scattered the thickest (fig. 217-a and illust. I, p. 180); at times the latter are so soft and vascular that they appear like blood clots and blood filled cavities; in other cases (as in fig. 217-a), *e.g.*, in the femur of a child, the metastases of a periosteal round cell sarcoma were white, homogeneous and like marrow. Osteo-

FIG. 214.—Numerous metastatic carcinoma nodules from primary adenocarcinoma of thyroid of 29 year old woman (r. lung frontal section surface, anterior half, hardened in formalin). Massive infiltration of lymph nodes; others, anthracotic partially carcinomatous or not at all; ½ nat. size.

sarcomas are also not infrequent, (Le Count). All the metastases mentioned may acquire considerable size; their histological character depends on that of the primary tumor. Fragments of metastatic nodules ruptured into bronchi may be expectorated, *e.g.*, in a 51 year old man with 1½ years of increasing dullness over the left lung, 5 years previously a left orchidectomy for polymorphocellular sarcoma; the same diagnosis was made from the expectorated material.

The relatively frequent (Scheidemantel, Hitschmann and Christofoletti) metastases of malignant chorionepitheliomas (fig. 215 and under brain) are exceedingly multicolored, white, yellow, brown and red, and

are characterized by large blood lacunae, vascularization and necrosis. Sometimes the lungs as a whole are peppered with miliary embolic tumor plugs (Brasche). The nodular metastases of endotheliomas of the pleura may also be hemorrhagic. In chorionepitheliomas, Marchand showed that from nodules formed by embolism, further dissemination is preferably through the peribronchial and perivascular lymphatics, but that numerous veins may be perforated. In a pleural endothelioma, the author observed the same spread through the lymph channels with subsequent rupture into blood vessels and bronchi (p. 494).

(*b*) Metastases may take the form of cords or nets or more rarely diffuse infiltrations.

The first frequently come from the pleura (carcinoma of the breast) or from bronchial lymph nodes (carcinoma of the stomach and esophagus,

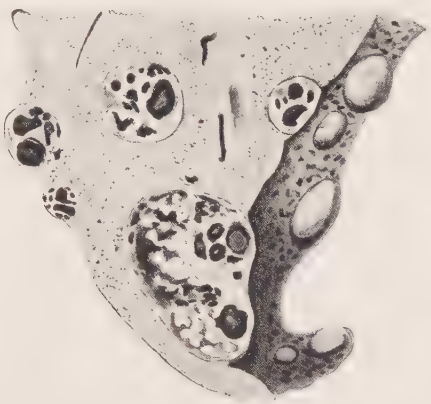


FIG. 215.—Metastases in lung and pleura from a chorionepithelioma of uterus (see illustr. under uterus and brain). Other lung metastases reached the size of a hen's egg. The woman had cough and hemorrhagic expectoration; $^{9}/_{10}$ nat. size.

etc., uterus, ovaries and even the prostate), retrograde against the lymph current which normally is directed toward the lymph nodes. In extension by continuity the cells progress in the pulmonary lymph channels sometimes in broad strands, more often in extremely delicate networks with nodules at the junctions; the pleural lymphatics may look like rosaries. Both lungs may be involved without the presence of larger nodules; pleural adhesions are absent, but nodules may be present on the serosa. The cells frequently line the alveoli or fill them completely, forming foci resembling miliary bronchopneumonias. Larger alveolar infiltrations resemble caseous pneumonia. The smaller bronchi and vessels are often narrowed by pressure or infiltrations in the submucosa and mucosa (vessel walls). More sharply defined nodules around the bronchi (peribronchial) resemble similarly situated tuberculous processes, and look like miliary tubercles. The term for this condition is lymph vessel carcinoma; carci-

nomatous lymphangitis is less satisfactory. When wide spread, it causes clinical symptoms, such as cardiac insufficiency, emphysema and dyspnoea (Bard, Meyenburg, x-ray pictures by Weil). Macroscopic strands are sometimes seen in secondary lymphosarcomas (observation, p. 279), when the primary tumor is usually in the nodes of the neck or mediastinum, as in sarcomas of the mediastinal nodes, or especially in the distinct hemorrhagic nodules of primary so-called endothelioma of the pleura. These latter invade the lungs from the pleura or from the hilum, follow the septa

FIG. 216.—Metastatic carcinoma of pulmonary lymphatics of 51 year old woman. 1½ year previous amputation of carcinomatous breast. (Metastases in liver and bones); ⅘ nat. size.

or travel into the interior of the lung along the bronchi and arteries as thick stenosing sheaths. Erosion of vessels leads to hemorrhage (observation, p. 494). Since they also infiltrate and erode the bronchial mucosa, they may be mistaken for primary bronchial tumors, when those in the lymph nodes or pleura are considered secondary.

In lymphogranulomatosis (p. 267) extension takes place also in the perivascular and peribronchial connective tissue; destruction or obliteration of bronchi and even rupture into alveoli has been observed (Ceelen, Rabinowitsch).

Hematogenous metastatic distribution occurs in sarcomas and enchondromas (*e.g.*, of the pelvis) by rupture of the primary tumors into veins

and subsequent embolism into the pulmonary artery. In carcinomas likewise the embolic route is sometimes chosen. At times metastasis is indirect by way of the thoracic duct (p. 183). Hematogenous metastases are rounded like ordinary metastases, without demonstrable embolism, or are like infarcts with carcinoma cells in the branches of the pulmonary arteries (p. 167) and thus are approximately wedge-shaped, or miliary in character (rare). Miliary carcinomatoses disseminated by the blood route are usually confined to the lungs; if general, the dissemination must

FIG. 217.—a, Numerous sarcoma metastases in right lung of a 10 year old child. Small round cell sarcoma (see illust. I, p. 180); starting point, retroperitoneal. OL, upper; ML, middle; UL, lower lobe. Left lung similar; ¾ nat. size.

have occurred through a pulmonary vein in a manner similar to general miliary tuberculosis. According to M. B. Schmidt, microscopic embolism is frequent in the arteries of the lung, probably via the thoracic duct (but according to Deelman, more likely via the direct blood route); but most carcinoma cells perish, are destroyed, or at least inhibited in their growth by nutritional disturbances and possible protective substances of the body. Carcinomatous thrombi and polypoid plugs may be present within the arteries while their walls show carcinomatous infiltration, *e.g.*, in a lung, macroscopically free of tumor (carcinoma of the esophagus), the infiltra-

tion of the walls of the pulmonary artery made it appear as though artificially injected.

Finally, embolism may produce simple hemorrhagic infarction, but the plugs in the arteries, though they resemble ordinary thrombi, enclose microscopically demonstrable carcinoma cells. Undoubtedly, therefore, an embolic miliary carcinoma does occur, but it is very rare. The lymph route, even retrograde transport from the bronchial nodes, is so much more frequent that most miliary nodules of the lung may be assumed to occur in lymph vessels, even in the cases in which all conditions seem favorable for embolic dissemination. In a man 50 years old with gastric carcinoma, the author saw rupture into the thoracic duct, the cloudy contents of which contained tumor masses. The lungs were filled with innumerable small nodules giving the impression of hematogenous origin, but microscopically the nodules were in dilated lymph vessels and it must be assumed that this occurred by retrograde transport from the infiltrated nodes of the hilum.

Some tumors reach the lungs from without, and by displacing them, appear to invade them; among these tumors are chondromas and sarcomas originating in the ribs or spine, malignant, deeply situated goiters, lymph node tumors, etc. (Large aneurysms of the aorta may also compress the lungs.) But other tumors, *e.g.*, carcinomas of the esophagus, directly infiltrate the lung or bronchi.

Rupture of tumor nodules of the lung into the pulmonary veins carries their fragments into the greater circulation (secondary embolism). Sometimes particles are caught in the auricle or ventricle (auriculo-ventricular valves) or even the internal surface of the aorta, where they may be engrafted (pp. 84, 85, etc., fig. 35).

See Meyer, and lit. p. 323 in reference to tumor-like amyloid deposits in the lung. See Kschischo (lit.) for participation of the lung in general amyloidosis (rare).

### Parasites of the Lungs

**Vegetable Parasites. Pneumomycoses.** — Pneumomycoses are colonizations of fungi in the lung. They consist of fission fungi, among which have been mentioned the pneumococcus, tubercle bacillus, etc. Among non-pathogens might be mentioned sarcinae and micrococcus tetragenus, the latter present in cavities and abscesses with tubercle bacilli and streptococcus pyogenes. (Tetragenus is pathogenic for white mice and guinea pigs, and is sometimes present in normal sputum.) In the relatively rare infections with hyphomycetes pathogene streptothrix (exclusive of the clinically and anatomically well defined actinomycosis, p. 467), a purulent bronchitis and bronchopneumonia is produced with tubercle-

like peribronchitic nodules in some cases, (streptotricheal pseudotuberculosis of man, Flexner). The conidia grow in long threads. Abscesses, cavity formation and bronchiectases are final results. The process may spread to the pleura and to neighboring organs. If healing takes place, the bronchiectases usually remain; but invasion of fungi into the blood stream produces pyemia with metastases in the central nervous system, etc., (Lohlein, lit., and Foulerton). There are thread or mold fungi such as aspergillus niger (lit. by Risel) and fumigatus (lit. by v. Hellens), the spores of which enter the lung by inhalation (as far as the alveoli), develop into threads and multiply, provided they receive sufficient oxygen. The first named produces flat vegetations or coatings of dark green color; the latter are blue green to ash gray. These fungi are by no means frequent, and very rare in an intact lung, but do occur in existing pathological changes which are chronic in their course (p. 410). Thus, they are found in bronchiectases containing secretions; the fungi appear in the sputum in coiled masses, or in cavities, abscesses, gangrenous foci, infarcts, sometimes in pneumonia. Influenza seems to favor their colonization (Muller, Kleberger). If the threads are thickly strewn, they produce inflammation (exudate) with subsequent yellow or gray yellow, dry friable, necroses. Cavities develop from liquefaction of the dead tissues. Nevertheless, recovery is the rule. Mucor, eurotium and oidium (mold fungi of a low order) are sometimes found under similar conditions. In a case described by Paltauf, fatal general infection took place (lit. in appendix).

**Animal Parasites.**—Echinococcus hydatidosus (see under liver) is rare as a primary invader, and is usually secondary from the liver through the diaphragm into the lung. The cysts vary in size. The surrounding lung tissue reacts to the invading echinococcus in different ways, either by productive inflammation surrounding the echinococcus with connective tissue or by abscesses and cavities. Adhesions between the pleural surfaces are practically always present in large cysts and perforation into the pleural cavity has occurred. Cysts have ruptured into the bronchi, so-called cavity hydatid cysts in contradistinction to closed cysts, whereupon the vesicles appear in the sputum or the individual dies of asphyxia. The entrance of air produces a so-called pneumocyst (Deve, lit., Escuredo, Arnstein, lit.). Echinococcus multilocularis is very rare as a primary invader of the lung (Hauser), since it usually comes from the liver through the diaphragm by continuity into the bases, although hematogenous metastases in the lungs are described (very rare). In Biber's case (lit.), all the lobes of the lungs were filled with numerous, hard, white yellow, sharply circumscribed nodules the size of a hazelnut to a walnut favoring the peripheral parts; there was no ulcerative disintegration in contradistinction to the condition in the liver. Distomum pulmonale (Westermann)

causes inflammations and pulmonary hemorrhages, and is frequent in Japan and China, (Katsurada, lit.); in Europe it occurs only in introduced cases. Diagnosis is made by the demonstration of ova in the sputum. The flukes and ova are found in other places such as the pleura, liver, bowel wall and even in the brain (Seifert, lit., Abend, lit.). Cysticerci (small vesicles), pentastomum denticulatum (see parasites under intestines) are rare.

## THE PLEURA

The pleurae are two transparent sacs of connective tissue lined by cells called epithelial or endothelial. The pericardium lies between the two pleural cavities. The portion covering the lung is called pulmonary or visceral pleura; the part attached by subpleural or peripleural connective tissue to the inner surface of the ribs and intercostal spaces is called the costal or parietal pleura, while the diaphragmatic pleura covers the upper surface of the diaphragm. The mediastinum is bounded laterally by the pleura. The pericardium lies within the mediastinum but does not fill it completely; the remaining anterior and posterior free spaces are called mediastinum anterior and posterior. Numerous lymphatics course under the pleura into the lymph nodes of the hilum; chronic inflammatory changes are frequent. The visceral pleura shows a regular etching and black pigmentation following the lymphatics often corresponding to the lobules (p. 420). In reference to the anthracotic intercostal markings, see p. 420. The pleura has great powers of absorption (Grober) of liquid or corpuscular elements (including bacteria) (Koch and Backy, Aoyama). According to Boit, the pleural endothelium can destroy bacteria by phagocytosis and bacteriolysis. [For methods of removal of particulate matter in endothelial cells, see Karsner, H. T. and Swanbeck, C. E., J. Med. Res., 42: 91: 1920.—*Translator.*]

**Hydrothorax.**— Hydrothorax is a collection of clear, amber colored serous fluid in the otherwise unchanged pleural cavity. It is not an inflammatory product but a transudate as in passive edema. It develops in the general hydrops of cardiac and renal lesions or hydremia, or as a result of local stasis edema of the lungs. Fluid in a pleural cavity obliterated here and there into compartments by old adhesions is a sacculated or multilocular hydrothorax. This naturally produces varying pictures. The adhesions themselves may become edematous and gelatinous, like jelly.

The consequences of such a collection (2 to 3 liters or more) are similar to those of an acute exudate (p. 488). When the thoracic duct is torn as from trauma, or when its lumen is narrowed from compression as from thoracic or pleural tumors, it may rupture and empty into the thoracic cavity producing a chylous hydrothorax; such fluid is opaque and white.

Purely chylous hydrothorax is very rare, but a chyliform hydrothorax is more common, *i.e.*, admixture of exudate or transudate with chyle (Jousset, lit.).

**Hemorrhages into the Pleural Surfaces and into the Pleural Cavity.**—Hemorrhages, usually as small petechiae and ecchymoses below and in the pleura are found, among other things, in death from suffocation, even intra-uterine. But ecchymoses are very often absent in death by asphyxia of the newborn because of intrameningeal hemorrhages (Kundrat). They also occur in various poisonings (phosphorus, arsenic, mercury), in severe infectious diseases, the hemorrhagic diatheses, and occasionally in cardiac deaths. They are of medico-legal value in violent suffocation if the external circumstances do not justify such an assumption and when no other cause of death is found (comp. P. Fraenkel). There is usually an unimportant extravasation of blood into the pleural cavity.

Larger hemorrhages (hemothorax) are caused by rupture of vessels due to trauma, as in penetrating wounds of the thorax (intercostal arteries) or tearing of lung tissue by fractured ribs, stab and bullet wounds, etc., or from rupture of an aneurysm (over 4 liters of blood have been found in the pleural cavity) as well as in tuberculosis and tumors (carcinoma, endothelioma, sarcoma).

If the pleural cavity is otherwise healthy the blood may remain fluid and be absorbed completely, but if it clots, organization begins and ends in adhesions between the two pleural surfaces (lit. by Deutsch and A. Israel).

Hemorrhage due to shell splinters shows a tendency to suppurate. When a serous exudate is added to the hemothorax, the fluid becomes more transparent, but remains red in color and absorption is greatly delayed (H. Burckhardt and Landois; Merkel).

Hemorrhagic exudates will be discussed under pleuritis.

**Pneumothorax.**—The pleural cavity is filled by atmospheric air (usually from a tear in the lungs) or, exceedingly rare, by gas developed from within (up to 2000 cc.). This latter may occur in a purulent exudate from an esophageal perforation or from a gastric ulcer ruptured through the diaphragm and pleura, etc.

Air may enter the pleural cavity in various ways: (*a*) from traumata, such as penetrating wounds of the thorax with or without injury to the lung, from the broken ends of ribs tearing the lung tissue, or (*b*) from spontaneous perforation as recent, quickly progressive tuberculous surface cavities (p. 450), or fresh abscesses, gangrenous foci, a subpleural necrotic focus (in influenza, Kundrat, etc.), infarcts (septic and common hemorrhagic; Hayashi), from traumatic or interstitial, at times vesicular (for instance in pertussis) or bullous emphysema; indeed, it may even arise from marked intrapulmonic pressure increase during spasmodic coughing,

sneezing and violent laughter (lit. by Liebmann and Schinz) and occasionally, from empyema of the pleura rupturing into the lung, *i.e.*, a bronchus. The consequences of the entrance of air are varied; in trauma if no bacteria are introduced, no pleuritis follows (simple pneumothorax); in spontaneous ruptures apart from those due to emphysema and the bursting of healthy lung tissue, organisms are usually introduced thus producing gangrenous pneumothorax. The exudate may amount to several liters. A gas-containing echinococcus cyst in the lung may simulate pneumothorax, (hydatid pseudopneumothorax. Deve, comp. Arnstein).

A closed pneumothorax is present when the opening, which permitted the air to enter, is blocked, whereupon the air is quickly absorbed, or remains in the pleural space for some time under considerable pressure. In an open pneumothorax the air passes in and out during respiration. When it enters the pleural cavity during inspiration and cannot be expelled on account of a valve-like opening (fibrinous membrane or tissue fragment), the term valve pneumothorax is used. This pneumothorax under tension is the most frequent form and is common after rupture of a cavity. The distension of the thorax and the pressure of the air may be very high; the air escapes with a hissing noise when the thorax is punctured.

In reference to the demonstration of pneumothorax during autopsy, see p. 452. A false pneumothorax develops from post mortem acid softening of the stomach and esophagus and entrance of gases into the pleural cavity. There remains a permanent pneumothorax if fresh air continuously enters the pleural cavity through a small opening often no larger than a pinhead.

Older adhesions, divisions or nooks (sacculated pneumothorax) vary the results according to the individual case.

In reference to the composition of the air in pneumothorax (increase of $CO_2$ even post mortem, diminution of oxygen, highest recorded intravital $CO_2$ contents, over 10% in closed pneumothorax), see Tobiesen.

Consequence of Pneumothorax. When much air collects in the pleural cavity, the elastic lung collapses, as when the thorax of a cadaver is opened, and the negative pressure is abolished, *i.e.*, the pressure on the lung and within the lung are balanced, or the tension of air in the pleural space may be high enough to compress the lung and expel all its air. The diaphragm is then pushed downward and bulges like a cupola into the abdominal cavity. In right pneumothorax the liver may be forced so far to the left that the gall bladder lies external to the left mammilary line, the mediastinal contents are displaced so that the heart is pushed towards the healthy side and backward; in left pneumothorax the left ventricle at autopsy may be found flattened, or indented like a saucer. Sudden death may result from displacement and kinking of large vessels (more details by Tendeloo).

According to the Forlanini Murphy process, Brauer and L. Spengler have introduced artificial pneumothorax in the treatment of pulmonary phthisis and bronchiectases. Autopsy findings have demonstrated healing—or atrophy—in the collapsed lung by connective tissue formation; the absence of oxygen injures the tubercle bacilli and their distribution is made difficult on account of the slowing of the blood and lymph circulation, (Bruhns; see experiments of Shingu). However, not many reports are at hand in relation to lasting results, (A. Schmidt, Tendeloo and Forlanini). The decisive factor in the success of such procedures is the condition of the other lung. According to Sorgo, pneumothorax does not produce favorable conditions for healing; rather it hastens the illness; Renon repudiates the treatment of pulmonary tuberculosis by artificial pneumothorax, but this view is possibly too hopeless in relation to suitable cases (unilateral diseases and healthy lung on the other side). (Schur and Plaschkes, Jessen, Jehn, Hymans-Josselin-Schut, Tendeloo.)

**Emphysema of Cellular Tissue (Emphysema of the Skin).**—For gas-gangrene of the skin, see under skin.

In emphysema of the skin air collects in the subcutaneous connective tissue giving a crackling sound on palpation; it may follow pneumothorax by ruptures through the soft tissues of the thorax, or more frequently, it is a complication of certain subcutaneous fractures of the ribs which tear the parietal pleural surface, the subpleural tissue, the visceral pleura, and the lung. Old adhesions of the pleural surfaces favor its development, for if they are present around the tear, the air is forced into them during expiration and from there into the subpleural and subcutaneous tissues. During each expiration, some of the air of the pneumothorax is driven back into the lung through the tear while another portion escapes through the opening in the parietal pleura into the subpleural and subcutaneous connective tissues. The air then proceeds further, elevating the skin like a cushion, especially in the neck, but later it is generally distributed over the whole body down to the lower thighs and knees. The author autopsied a case (numerous fractures of ribs and tears of the lung) in which the scrotum was distended to the size of a child's head, the penis as large in circumference as the colon and showed an S shaped curve; even the entire scalp crackled on palpation. Local emphysema of the skin sometimes appears after tracheotomy.

Pneumothorax rarely develops from a penetrating wound in the thorax which does not injure the lung, *i.e.*, by inspiratory intake of air from without. If the wound is closed during expiration, the air in the pleural cavity may be forced into the subcutaneous tissues.

Emphysema of cellular tissue may also develop in subpleural tears of the lungs; the connective tissue of the hilum is first infiltrated by air,

later the cellular tissue of the neck, etc. (see interstitial emphysema of lung, p. 369).

A general emphysema of the cellular tissues of the body occasionally develops from rupture of a tuberculous lymph node into a bronchus. At each inspiration, and perhaps also during expiration, air enters the peribronchial cellular tissue, spreads to the mediastinum, the connective tissue of the neck, etc.

**Inflammation of the Pleura. Pleuritis.** *Etiology.*—Pleuritis develops in many different ways. It may be (1) primary, *e.g.*, traumatic, or idiopathic, *i.e.*, the only local symptom of an infection, usually by pyogenic cocci and the diplococcus pneumoniae (Weichselbaum); it seems that the exudate, as a rule, is purulent and sometimes spontaneous absorption occurs in pneumococcic infections. Most forms of "idiopathic pleuritis" which the clinician meets, whether serous or purulent and without bacteria (Weichselbaum), are probably of tuberculous origin; this idea is supported by the results of animal experiments (Aschoff). Pleuritis may also be (2) metastatic in various infections such as pyemia, septicemia, articular rheumatism, typhoid fever, the acute exanthemata, infectious nephritis, etc. (3) Pleuritis by continuity comes from various pneumonias, pericarditis, mediastinal and bronchial lymphadenitis, carcinomas of the esophagus, aneurysms, caries of vertebrae or ribs, carcinoma of the breast with suppuration, peritonitis, subphrenic abscesses, splenic and liver abscesses, ulcerative processes of the stomach, etc. That following lung diseases is the most frequent form; it is a constant companion of lobar pneumonia, but often accompanies lobular pneumonias, especially purulent and gangrenous forms. Influenzal pneumonia tends to empyema (Wildegans, lit., Stich) with a special tendency to the formation of fibrin (von Beust, lit.). Embolic foci, infarcts, abscesses and other interstitial pneumonic processes may induce pleuritis. But tuberculous pulmonary processes are paramount in producing serous, fibrinous, and adhesive pleuritis.

Pleuritis starts with an inflammatory hyperemia; the lining cells of the pleura swell and proliferate and desquamate in large numbers. The lamellae are exfoliated and saturated with serum, fibrin, and leucocytes, while the surface loses its luster and the lymph vessels show the changes described under acute lymphangitis (p. 173). The histological changes correspond completely with those of pericarditis (p. 5 and ff.). The character of the exudate deposited on the surface distinguishes the various anatomic forms of pleuritis.

**Fibrinous or Dry Pleuritis.**—The pleura is covered by a more or less heavy layer of fibrinous exudate arranged in nets and leading to adhesions. This form, among others, often accompanies fibrinous and tuberculous caseous pneumonias.

**Sero-Fibrinous Pleuritis.**—The serous fluid is pure or mixed with considerable quantities of fibrin flocculate, desquamated lining cells and exudate cells. The cellular and fibrinous masses settle out in the cadaver, and the upper layers are clear.

**Purulent Pleuritis (Empyema, Pyothorax).**—This form develops either from the sero-fibrinous by an increase in leucocytes and gradual liquefaction and disintegration of the fibrin or it is suppurative from the beginning. See above under etiology. This type has a pronounced tendency to become chronic. The pus may undergo fatty degeneration and thicken to a caseous mass, usually devoid of organisms. The pleural surfaces, as a rule, are thickened, stiff, cicatricial and sometimes calcified.

Encapsulated acute empyemas may be surrounded by sterile serous transudates (Koniger).

The conditions subsequent to penetrating thoracic bullet wounds include a purosanguinous (chocolate-like) empyema, gas empyema, etc., (more details by Wieding).

**Putrid Pleuritis (Putrid Empyema).**—The pus laden exudate becomes gangrenous and putrid. It starts in a simple gangrenous, often tuberculous focus invaded by the organisms of decomposition. Usually a gangrenous pyopneumothorax is the complete picture.

**Hemorrhagic Pleuritis.**—Hemorrhages often occur in tuberculous pleuritis and in conjunction with malignant tumors of the pleura. The exudate in time becomes deep red; in the presence of tumors it may contain cell masses permitting diagnosis, *e.g.*, endotheliomas (see below). The pleuritic exudate often assumes a hemorrhagic character in the hemorrhagic diatheses such as anemia, purpura hemorrhagica, scurvy, icterus, etc.

**The Course of Exudative Pleuritis.**—A serous exudate may quickly disappear by absorption; exudates rich in fibrin require more time, but even they may be completely absorbed after molecular disintegration of the fibrin. If disintegration is delayed, however, a reactive inflammatory overgrowth occurs, and vascular granulations from the pleura penetrate the fibrin as a plastic pleuritis which may follow any form of acute pleuritis, (comp. productive pericarditis, fig. 2 and p. 8). It leads to nodular, flat and broad, stringy, or tape-like pleural adhesions (pleural synechiae). Numerous such adhesions cause marked distortion of the lung; flat, broad synechiae obliterate the pleural cavity. Sometimes the fluid or a thickened exudate is encapsulated by adhesions (encapsulated pleuritis), but this is not the same as collections of edematous fluid in the meshes of a network of adhesions. Thickening is so marked at times from continuation of the plastic inflammation that the fibrous shells measure 0.5 to 3 cm. They consist of homogeneous dense connective tissue, often hyalinized. The pleural surfaces may be completely fused and the adhesions

are so firm that it is impossible to detach the costal pleura at necropsy. In such cases the lung must be cut out which is very troublesome; it is advisable to saw through the ribs laterally from above downward and remove them with pleura and lung; this secures good topographical specimens. Sometimes a very firmly adherent lung may be taken out by removing the organs of the neck in conjunction with the lungs; this allows a good grip and the apices of the lungs can be reached more easily from behind and freed by the knife. Calcification is common. The combination of all these changes often justifies the term deforming pleuritis. Peripleuritis may follow pleuritis, the bordering lung septa become thickened (interstitial pneumonia), most frequently in the lower parts of the lungs.

Partial calcification is also not rare, especially in the parietal pleura as flat white so-called pleural bones, consisting, however, of dense calcified connective tissue and only occasionally of true bone which is light gray to yellow in color.

Some hyalin fibrous thickening may contain cartilage (or bone) as smooth confluent drops (similar to porcelain) or as oddly shaped, nodular, coralline, fibroma-like formations.

**Consequences of Pleuritis.**—If the acute exudate is fairly abundant (half a liter or more), the lung is compressed; when more is present (2, 3 to 5 liters), the air and blood are completely pressed out of the lung which becomes small, airless, bloodless, flabby, but tough and lead gray in color. It is displaced backward and pressed flat against the spinal column; even the bronchi may be kinked. In unilateral collections the mediastinal wall and the heart may be pushed to the healthy side. When adhesions are quickly produced the exudate is prevented from rising, or older adhesions may encapsulate the fluid, *e.g.*, if the collection occupies the lower pleural cavity it forces the diaphragm downward; between the base of the lung and the diaphragm it is difficult to demonstrate clinically. The thorax is distended on the affected side, the chest becomes asymmetrical, the diaphragm is pushed downward, the abdominal organs are displaced, the intercostal spaces and even the ribs bulge outward. This may all disappear if the exudate is absorbed quickly enough or is removed by puncture (thoracocentesis) or thoracotomy (usually by resection of ribs); the relieved lung reexpands.

But if the pleuritis becomes chronic, the lung is permanently damaged by a chronic interstitial pneumonia (fig. 188), or by failure to reexpand because of adhesions, or by the compression of shrinking scar tissue (collapse induration, fig. 203).

Since a chronic pleuritis destroys the lymph channels, the spontaneous removal of an exudate by absorption is almost impossible. Larger sup-

purative exudates, if untreated, are fatal from cachexia and pyemia, especially in children; a poor hope is spontaneous expulsion by ulcerative rupture and perforation through an intercostal space or through a carious rib. In some cases the perforation is external usually close to the sternum where the soft tissues are thinnest; the skin becomes reddened as a premonitory sign, thinned and finally perforates. Internal perforation is much rarer into the pericardium, the mediastinum, through the diaphragm into the abdominal cavity, or into a bronchus after erosion and suppuration of the lung; the exudate is then expelled in the sputum and a pneumothorax is established. According to Ad. Schmidt, the rupture of small encapsulated empyemas into the lung is not at all rare (p. 483) with subsequent slow discharge in the sputum (Liebmann and Schinz).

**Thoracic Contraction (Retrecissement thoracique).**—When, in the presence of a productive fibrous pleuritis, an exudate (usually pus) is removed by spontaneous perforation or by operation, the walls of the pleural cavity shrink until the soft tissues (diaphragm, mediastinal walls, heart) and even the stiff thoracic wall are pulled in, provided that the lung of the diseased side has lost its power of expansion. Consequently, on the diseased side the diaphragm is high, the intercostal spaces contracted, and the ribs fixed like shingles over each other and finally convex internally until there is a deep depression in the thoracic wall. The spine shows scoliosis convexity to the healthy side, the healthy half of the thorax is distended in compensation and the lung is, as a rule, emphysematous. This constitutes a high degree of thoracic asymmetry (see p. 468 under actinomycosis).

**Infectious Granulation Tumors. Tuberculous Changes in the Pleura.** Two types may be distinguished: (*a*) true tuberculosis of the pleura, consisting of nodules and (*b*) a tuberculous pleuritis, with nodules and other inflammatory processes.

(*a*) Tuberculosis of the pleura is usually derived from the lungs, caseous bronchial lymph nodes, caries of ribs, spinal column or from the abdominal cavity. It is occasionally seen in acute general hematogenous miliary tuberculosis when the nodules are of miliary or submiliary size and frequently so numerous and small that the pleura looks as if covered with sand. When larger, they have a hyperemic halo. In other cases there are larger caseous, dry, yellow clumps formed by confluence resembling bovine tuberculosis.

Tuberculosis of the pleura and other serous membranes in cattle is distinguished by rounded nodules which vary greatly in size but are sometimes as large as a potato, gray red in the beginning, then yellow, opaque, dry, caseous, caseous fibrous, or fibrous calcareous, often connected with each other by fibers, or strung like pearls on a thread and attached by con-

nective tissue fibrillae to the pleura (fig. 218-b); others close together, form larger caseous masses. Peculiarities of the nodules are the abundance of giant cells in fresh growths and the tendency to caseation and quick extensive calcification and fibrous metamorphosis, unique in comparison to the tuberculosis of man. The nodules contain the bacillus of bovine tuberculosis which is said to be identical with the tubercle bacillus of man (v. Behring, Romer, Ruppel and others; lit. by Pertik and for which among others, the experiments of Schottelius, Esser-Orth, Fibiger-Jensen, Eber, etc., are quoted in support). In reference to the value of these experiments, see

FIG. 218.—Bovine tuberculosis of pulmonary pleura of a cow; ½ nat. size.

the critique of Tatewossianz, lit. But Robert Koch, at the International Tuberculosis Congress in Washington, 1908, maintained the stand expressed in London, 1901, against Nocard, Jong, McFadyen, that the organisms which cause tuberculosis in man and in cattle are not identical; the latter he admitted were transferable but of rare pathological effect on man. It is opinion against opinion in reference to the constancy of morphologic, biologic and pathogenic differences between the bacillus of human and bovine tuberculosis (Kossel, Weber, Heuss, Schieck and others); in reference to the essential nature of the differences, *e.g.*, the bovine type is much more virulent for rabbits, which die in 5 to 6 weeks after inoculation (English commission, Rabinowitsch, Beitzke, Parodi, Fibiger-Jensen, Eber) or is it because of variations in one and the same organism? (Much-Eug. Fraenkel); see Mietzsch, Ref. Beitzke, Park-Krumwiede.

So-called intermediary forms (between human and bovine) are often found in lupus (see under skin) (English commission). It is now certain that human tuberculosis can be experimentally transmitted to cattle and the bacillus of cattle (sheep, goats, pigs) can be infectious to man, but it is as yet undecided whether the latter infects only children (Kossel, Weber, deBesche, Beitzke) with intestinal and mesenteric lymph node tuberculosis, mostly confined to the portal of entry and the regional lymph nodes, often healing and rarely causing death by severe intestinal disease, meningitis, or generalized tuberculosis, or whether the bovine bacillus can infect adults and whether it does play a part in the development and spread of human phthisis. The latter has been flatly denied by R. Koch (Mollers, lit.); to him the tuberculous human being is the main source of further infection, (H. Burkhardt, lit.). In reference to the danger of bovine tubercle bacilli in lupus tuberculosis of the cervical lymph nodes, etc., comp. the opinions of Eber, Orth, Rabinowitsch, Hart and Rabinowitsch.

(*b*) The appearance of tubercles is accompanied by inflammation; *i.e.*, exudation and tissue proliferation. It is sometimes primary, but usually secondary to the same conditions as the simple nodular form. Tuberculous processes of the lung may be quite mild and clinically overlooked.

The quantity and character of the exudate vary; it is often serous or sero-fibrinous (abundant –up to 4 liters) or hemorrhagic, which is the rule in primary tuberculous pleuritis. The pleura, coated with fibrin, proliferates and the granulation tissue reveals numerous tubercles in the form of minute gray nodules; the granulations are very rich; delicate blood vessels rupture and cause the hemorrhagic character of the exudate. Very vascular flat or corded adhesions contain minute nodules arranged in rows. The exudate may dry and become caseous, but in other cases, usually with threatened or completed rupture of cavities, the exudate is suppurative or sero-purulent containing neither pyogenic organisms nor tubercle bacilli. According to Weichselbaum, a suppurative pleural exudate without (or only by animal inoculation) demonstrable bacteria always points with great probability to tuberculosis. In still other cases only a little fluid is accumulated, the pleuritis is dry, fibrinous, but also markedly productive leading quickly to adhesions and fusions, and later to firm cicatricial bands especially at the apex, although also at the base. In the bosses and adhesions are miliary and conglomerate tubercles and sometimes caseous masses embedded in old adhesions. This form is exceedingly frequent in chronic pulmonary phthisis. Sometimes the caseous granulation tissue is so plentiful that it forms a layer 1 cm. thick (caseous pleuritis) which uniformly envelops the lung surfaces, is closely attached to the pleural surfaces and fills the interlobar clefts. Thick projecting caseous

rolls are also seen, especially on the costal pleura. Tuberculous abscesses of the thoracic walls may result (Iselin).

Inflammatory new growths with broad or pedunculated bases are quite unusual but produce a "fibro-tuberculous hypertrophy" which may assume immense proportions simulating a true tumor of the pleura (Rist and Ribadeau-Dumas, lit.).

Syphilitic pleuritis may appear in conjunction with gummatous conditions of the lung (Lissauer, lit.). Actinomycosis on p. 468. Lymphomas in leucemia or pseudoleucemia appear as diffuse infiltrations or nodules. They resemble carcinomas, the more so because they are hemorrhagic.

**Tumors of the Pleura (Lit. in Appendix).**—Primary tumors are rare. Benign tumors are usually fibromas, mostly of small size; lipomas derived from subserous fat, chondromas, osteomas, angiomas, etc., also occur. Malignant tumors are:

**Sarcomas** as disseminated nodules or a large connected tumor (very rare); among them are soft vascular angiosarcomas of quick growth, fibrosarcomas, chondromyxosarcomas, etc.

In a woman 29 years old the author found a soft sarcoma larger than a child's head occupying the lower part of the right pleural cavity. The lung was forced backward and upward, the infiltrated diaphragm was pulled down to the 7th rib, while the anterior and upper parts of the right pleural cavity were filled with sanguinoserous fluid and fibrin; paracentesis during life showed cellular masses diagnosed as sarcomatous. Microscopy: polymorphocellular large cell sarcoma; the cell masses formed actual coatings in many places around wide, thin walled vessels; many of the latter were occluded by thrombi; the tumor tissue was necrotic in many places; small metastases in the spleen, kidneys, liver. Mehrdorf (lit.) described an immense fibrosarcoma 3270 gms. in weight, which filled the right pleural cavity like a hard casing (interpleural) (42 year old woman).

Neuromas (better neurinomas—see there) and neurofibrosarcomas, cylindrical, slightly nodular, the size of a fist or very large, are clinically not malignant, see Grawitz (Banse). Myomas may spring from the smooth musculature of the pleura (Baltisberger). (Plasmocytoma on p. 272.)

Endotheliomas (for histology, p. 179) are rather rare. They are derived (*a*) from the endothelium of lymphatics and clefts (lymphangioendotheliomas) and (*b*) from lining cells. The first origin is supported by Glockner, Podack, Adler, Torri and others; the latter by Benda, Dreesen, Ribbert, Demole; the author believes in both. According to the author's experience, it is easier to conceive of the latter than the former.

Just as their derivation is disputed, so is the nomenclature of these tumors which cannot be differentiated macroscopically. Formerly they

were called endothelial carcinomas (Wagner-Schulz); we call them endotheliomas; some call (*b*) types of carcinomas (Ribbert, Demole, lit.) because the lining cells of the pleura are called epithelial, according to the coelum theory of O. and R. Hertwig. But according to later researches, the large serous cavities are produced secondarily by fissures in the mesenchyma; thus their lining cells are modified mesenchyme or connective tissue, appearing primarily in epithelial form but later as flat aggregates. These cells, on the one hand, may form fibers; on the other hand, by regeneration, they may produce perfect gland-duct-like proliferations. These epithelium-like forms we also see in the endotheliomas of the pleura which have been called mesotheliomas, or malignant lining cell tumors; the complete macroscopic picture has little in common with carcinomas elsewhere situated, often no resemblance at all.

They are flat infiltrations of the pleura, the latter participating in the form of a serofibrinous, often hemorrhagic pleuritis, which contributes by organization in changing the pleura into a thick, firm shell which is, microscopically, filled with tumor masses. Nodular and raised tumor masses may be prominent on the inner side of this sac (fig. II, p. 180). Single or multilocular sacs may be seen. The predominant symptom is chronic pleuritis. Several liters of exudate (often sero-sanginous) may compress the lung. In other cases on a pleura not yet thickened, are firm or softer nodules, lumps, or condyloma-like excrescences which may be covered by fibrin meshes and blood coagula, and, if small, may resemble tuberculosis.

In a man 36 years of age, the author saw the left pleural cavity changed into a sac the size of a man's head lined with lumps and plates and containing several liters of red watery fluid; the sac could be almost completely detached from the thoracic cavity.

Extension is often closely confined to the lymph channels and thus the lungs are invaded by peribronchial and perivascular stenosing and eroding tumors (hemopthisis). Occasionally there are diffuse infiltrates or rounded nodules in the lungs (as in a woman 70 years old). Another time the extension goes to the intercostal muscles (rare), the pericardium (rare), and through the diaphragm to the peritoneum (liver, intestines, etc.). The broncho-tracheal nodes are much infiltrated, discolored red, brown, white or yellow speckled, and sometimes they transmit the tumor from one pleural cavity to the other. There are also true metastases by way of the blood, although rarely (lit. by Monckeberg). A left endothelioma of the pleura in a cachectic man 53 years of age produced 800 cc. of exudate in the pleural sac which was lined with nodules histologically like adenocarcinoma with extensive necroses in the gland-like formations; there were no metastases to lymph nodes, but many small nodules in the right lung, both kidneys, liver, brain, and skeleton, the latter with ossifying characters and

compression of the lower thoracic and lumbar spinal cord. Podack saw secondary nodules in puncture wounds (clinical by A. Frankel).

In a 63 year old man with the symptoms of sero-hemorrhagic recurrent pleuritis, there was found a tumor partly as diffuse, white red, firm infiltrations of the costal and the right diaphragmatic pleura, partly as softer circumscribed nodules and excrescences on the visceral pleura, and partly as firm nodules on and through the diaphragm to the peritoneum on the right side continuing to the cecum where there was a hard mass almost as large as a fist; metastases without continuity were not found (microscop. see pp. 179 and 180, figs. II, III, IV).

In a 54 year old man who 4 weeks previously had painful swelling of the cervical lymph nodes, blood in the sputum, difficulty in swallowing and rapid loss of weight, left pleural puncture obtained a sero-hemorrhagic fluid, containing clumps of round and oval cells undergoing fatty degeneration. At autopsy the left pleural cavity contained 3800 cc. of sanguinous fluid; its inner surface, especially the diaphragmatic pleura, was studded with innumerable flat, soft, tumor masses the size of lentils and peas, but usually smaller; thicker, firmer, red, flat growths were covered by fibrin and resembled a hemorrhagic tuberculous pleuritis. There was immense enlargement of the broncho-tracheal and even the abdominal lymph nodes with speckled discoloration. Radiating from the hilum, from the pleural surface and following vessels and bronchi, was an infiltration of the lung accompanied by stenoses and corresponding distal ectasias of bronchi (containing mucous spirals) with approximately 12 erosions of bronchi and arterial vessels; much blood in the bronchi. The lung tissue was invaded in many places by blocks of tumor tissue to the size of walnuts which were directly connected with the lung infiltrates. The tumor was quite variegated from blood, necrosis and fatty degeneration. The spleen showed two small metastatic nodules.

**Secondary Tumors.**—Various tumors in the neighborhood may continue into the pleura. Apart from rare benign tumors, they are chiefly carcinomas, sarcomas and lymphosarcomas. Carcinomas may cause diffuse infiltration, injections of lymph channels, distinct nodules or rounded prominent bosses. In a carcinoma of the os uteri (51 year old woman), and a carcinoma of the breast (39 year old woman), the author saw numerous, radiating, cicatricial, contracted metastases of the pleura, giving the surface of the lung a lobulated appearance (see similar findings and illust. by Ribbert). Carcinoma of the pleura develops most frequently in conjunction with carcinoma of the breast and stomach. Lymphosarcomas which start from mediastinal or bronchial lymph nodes may extend to the pleura by diffuse infiltration of the lymphatics. A unilateral endothelioma of the pleura may secondarily invade the other side.

Carcinomas and sarcomas produce hematogenous metastases quite rarely. Oberndorfer described a metastatic sarcoma filling one-half of the thorax from a primary sarcoma of an extremity (see the case of Grabow, and his lit. in reference to primary tumors of the pleura).

In most primary or secondary malignant tumors of the pleura of larger extent, there is a serofibrinous, or perhaps more frequently, a serous pleuritis of hemorrhagic character (at least with endotheliomas).

In reference to the diagnosis of tumor of the pleura by the examination of aspirated cells, Dufour's experience must be remembered; this showed that numerous desquamated lining cells may be found in the pleural exudate without metastases, vacuolated perhaps from the carcinoma dyscrasia; these may easily be mistaken for tumor cells. According to the experience of the author, the differentiation can usually be made, since the cells of both primary and secondary sarcomas are much more irregular, larger, with larger nuclei, while in endotheliomas and secondary carcinomas the cells are less polymorphous and usually lie side by side in larger clumps.

Grossly, carcinomatous pleuritis at times markedly resembles tuberculous pleuritis, because in some carcinomas there is dissemination of innumerable nodules similar to miliary tubercles without inflammation.

**Animal Parasites.**—Echinococcus may be primary (lit. by Maydl and E. and M. Vincent) or secondary to rupture from the lung, or from the liver or spleen through the diaphragm into the pleural cavity.

### Appendix to the Respiratory Organs

**Thymus (and Anterior Mediastinum).**—The development (fig. 219) and anatomy are replete with controversies (lit. by Hammar and by Matti). According to Hammar, the thymus gland is an epithelial organ filled with lymphocytes; according to others, it is a lympho-epithelial organ but different from pure lymphoid structures such as the spleen and lymph nodes, (Mollier). According to Stieda, it develops from the (entodermal) third branchial cleft as a paired, originally hollow, tube with thick walls consisting of elongated epithelial cells; this tube ramifies, becomes lobulated, and the caudal ends fuse to an apparently simple structure. Then histological metamorphosis sets in by invasion of the thick epithelial walls with (mesodermal) lymphoid connective tissue and blood vessels which gain the upper hand in the 2nd and 3rd months so that the structure resembles a lymph node. The internal lighter parts are the medulla, the outer parts with thickly strewn, small round thymus cells, the cortex. Among the motile cells in the scanty developed reticulum are small round cells, closely packed side by side in the cortex; they resemble lymphocytes, and are so called by Schaffer, Maximow, Hammar,

Hart, Pinner, Marchand, and others, while Stoehr, Schridde, Fulci, etc., consider them derivatives of epithelium. Against Schridde's views, Pappenheimer demonstrated lymphocytic granules in the small thymus cells. In a network of more or less branching epithelial cells in the medulla, are relatively large, oval or rounded cells, among them eosinophilic leucocytes, and also the corpuscles of Hassal (Schaffer). From the discovery of nucleated erythrocytes it was supposed that the thymus belonged to the hemopoietic organs; Maximow thought it was a source of lymphocytes, Weidenreich of non-granular and granular leucocytes, but this and that view is much disputed. The epithelium is obviously preserved only in Hassal's corpuscles, concentrically laminated bodies, situated in the medulla, which show central fatty degeneration, or cornification (doubted by Hart) or calcification. Microscopically, they resemble epithelial pearls (cancroid pearls). They can be 0.5 mm. in diameter, and can be recognized macroscopically as white dots. Hammar thinks they are formed by the interlocking of numbers of hypertrophied reticulum epithelial cells since he, in conformity with Stoehr, considers the thymus an epithelial organ with internal secretion (endocrine gland). Hart speaks of medullary cells in contradistinction to cortical round cells (other views by Schambacher). In reference to transverse striated cells, see Weissenberg; for lymph follicles with germinal centers in the medulla of the thymus in status lymphaticus, see p. 499, and Pettavel, Wegelin.

Its weight in the fully matured newborn infant is 14.3 gms. according to Friedleben; according to Hammar, 13.26 gms. The "secretion," a pus-like juice, is most abundant in the first nine months of life. The organ enlarges up to the time of puberty (about 14–15 years) and reaches a maximum weight of 37.52 gms. according to Hammar (but see Soderlund and Beckmann). According to Klose and Vogt, it ceases to enlarge at the end of the 2nd year. On cross section, it is found lobulated (small) like a salivary gland, in contradistinction to the homogeneous lymph nodes. It is situated anterior to the pericardium and the large vessels behind the sternum in the anterior mediastinum and spreads upward in two prolongations which reach the thyroid gland. At the beginning of puberty its weight decreases (involution of age); at the 25th year it weighs about 25 gms., and from 66–75 years approximately, 6 gms. During these stages it regresses into a retrosternal fat lobule (thymic fat body, Waldeyer) by general parenchymatous atrophy and proliferation of fatty tissue; microscopically, however, traces of lymphoid tissue and Hassal's corpuscles can probably be demonstrated in the fatty body (Sultan) so that the thymus is preserved throughout life as traces of parenchyma (Ronconi, Barbano, Hart). For thymus cysts in senile atrophy, see Tamemori and others. The thymus persists but rarely during life behind

the manubrium as a red white structure with as much parenchyma as in its highest developmental stage and without noteworthy modification from the normal (Schridde), the so-called persistent thymus or incomplete involution (Simmonds) or subinvolution (Hammar) (comp. Yamanoi). It may easily be mistaken for a hyperplasia, *i.e.*, its abnormal size may be considered a recrudescence or redevelopment at the respective age.

When the cornuae persist, the thymus extends in adults to the thyroid gland, which is by no means rare; if merely parts remain they are called accessory thymus glands usually near the thyroid gland.

See Gruber in reference to variations in the shape of the thymus.

**Physiological.**—The results of extirpation of the thymus in animals depend on the time of operation, whether during maximum development or later. In adults it has practically no influence, while in very young animals the influence is considerable: (*a*) temporary interference with the development of the testes; conversely castration allows the thymus to gain weight (Calzolari, Henderson, Goodall, Squadrini, Soli, lit.), so that Tandler and Gross assume the thymus initiates puberty at the proper time; (*b*) disturbance of growth of bone, hypoplasia, flexibility, fragility, atrophy of skeletal musculature, injury to ganglion cells and nerve fibers of the brain (Basch, Soli, Klose). Matti (lit.) especially, emphasizes the resemblance to rickets which in fact is considered by Klose to be due to inhibition, or severe injury to thymus function (Kranz likewise), but Hart sees no specific effect of thymectomy, merely a consequence of weakening of the organism, and disturbed metabolism. Klose and Vogt distinguish 3 stages or sequelae of thymectomy in young dogs; in older animals the consequences are milder; the latent stage (2 to 4 weeks), the adipose stage (the following 2 to 3 months), the cachectic stage or cachexia thymopriva from the 3rd to the 14th month. They suppose the decisive factor in these changes is an acidosis, assuming that the thymus has a neutralizing activity through nuclear synthesis as a balance against the liberated phosphoric acid and its complicated compounds formed in the growing parts of the organism. They also believe the spleen is the main substitute for the thymus. While Flesch obtained fatal results in thymectomy on rats, Hart saw no life threatening effect, only a slowing of developmental progress and thus he believes the thymus is not an organ essential to life, but its removal checks the general proportionate development of the body, (thymus a growth controlling organ). There are relations between the thymus and thyroid (p. 501), the thymus and hypophysis (see there), the thymus and the adrenals (p. 501) and genitalia (p. 500); Leupold supposes the normal development of the testis is controlled by collaboration of thymus and adrenals. The general conclusion is that the endocrine glands are interrelated (lit. by Biedl, Soli; another

conception, for instance, Lucien and Parisot; lit. by Wiesel, Lubarsch). In animals both young and old, Fulci discovered a marked capacity of the thymus for regeneration, and in mammals a power of restitution after the involution due to pregnancy. According to Bompiani, suckling prevents this restitution.

For importance of the thymus in surgery, see Zesas, Capelle and Bayer, v. Haberer, etc.

Diseases of the thymus are rather rare; atrophy is frequent in children fed unsuitable or insufficient nourishment, in destructive toxic infectious diseases and in acute starvation (Johnson, lit.).

This is also called accidental or pathological involution (by Schridde, sclerotic atrophy) and consists of loss of weight, atrophy of the lobules first, especially of the cortex, and gradual and relative extension and sclerosis of the connective tissue between the lobules. The macrophages (reticulum cells) in a starvation thymus are loaded with fat droplets. Atrophy is also found in congenital lues, without, however, an increase in connective tissue (Hammar, Hart, another opinion by Schridde). According to Hart, the thymus is an index of general nutrition. Involution must be considered carefully in giving data as to normal weights.

Thymus aplasia has been observed very infrequently (Hart).

Thymus hyperplasia is important, according to some chiefly of the cortex, according to others the medulla; it has been held responsible for some sudden deaths in suckling infants and children, also in older individuals with large thymus glands (death of soldiers while swimming, cold bathing, etc.). Its weight may be more than 50 to 70 gms.

**Two Eventualities Must be Distinguished.**—(1) The hyperplasia is considerable and causes death, usually suddenly, by asphyxia (thymus death—mechanical thymus death); suckling infants and children with status thymicus, as a rule, have several attacks of asphyxia before the fatal one. There is compression of the trachea, most frequently where the innominate artery crosses the trachea obliquely, corresponding to about the upper thoracic aperture. This relation can be best demonstrated in a formalin preparation hardened in situ (disputed by v. Sury). Since Barack and Flugge called attention to this form of compression, a number of such observations have been recorded (cases of Hedinger, also cases without changes in the lymphatic apparatus!); also the operative results of thymus stenosis *i.e.*, stenosis of the air channels caused by a large thymus (lit. by Rehn, v. Haberer), support the correctness of the above view. The author, *e.g.*, reported such a case in a 3 months old girl. Barack, Ducrot and Hedinger (lit.) found a familial occurrence in such cases and the lymphatic apparatus is not necessarily hyperplastic. Other cases are interpreted as heart deaths from compression of the large

vessels (lit. by Christeller). If there is also hyperplasia of the lymphatic apparatus (see under 2), the enlargement of the thymus is usually less marked, and the sudden deaths observed in these cases cannot be explained as mechanical, but due to causes mentioned under 2. A fairly well marked strumous condition is also rather frequent. The importance of this combination requires consideration in diagnosing the cause of death, since there occur congenital goiters which cause death, usually soon after birth, by compression of the trachea; in cases of the latter type the author observed familial relations. Thymus death is conceived in this way: the vascular organ, as large as a fist or more, is markedly engorged and exerts direct pressure on the trachea; sudden backward bending of the head causes swelling of the veins of the neck, a pull on the trachea and acute compression by the swollen thymus. Others (for instance, Grawitz) believe that the fatal tracheal compression occurs at the thoracic entrance. The enlarged thymus is also supposed to cause respiratory impediment by pressure on nerves, for instance, the vagus, or the recurrent laryngeal, producing spasm of the glottis (thymic asthma). But anatomical proof of this event is lacking and the absence of such symptoms in the presence of true tumors speaks against it. Lit. in reference to mechanical thymus death by Wiesel, Schoppler, Peretz-Montaut, Christeller.

(2) Mechanical thymus death is contrasted by sudden death which cannot be charged against stenosis by the thymus but in which, as a rule, a status thymo-lymphaticus (Paltauf) is present, *i.e.*, status lymphaticus added to status thymicus (v. Haberer). Both do not necessarily belong together; there is a pure status lymphaticus without hyperplasia of the thymus (Schirmer) and conversely, as stated above (Hedinger), a true status thymicus without association of the lymphatic apparatus. To this extent, the teaching of Paltauf has been corrected, according to which thymic hyperplasia is only part of a hyperplasia of the whole lymphatic apparatus; in addition, the thymus is no longer considered a lymphoid organ, but epithelial in character.

Status lymphaticus observed in the newborn (Schridde, Schirmer, lit.), but more frequently in children and youths, consists of a congenital lymphatic "constitution of the body" which must, however, be differentiated from the lymphatism acquired by infection or other causes. The hyperplasia involves various parts of the lymphatic apparatus such as the lingual follicles, tonsils (Schridde, J. Bauer), the laryngeal tonsils (Imhofer), the pharynx, lymph nodes, intestines; there are also deviations in the structure of the lymph nodes (Bartel and Stein), enlargement of the spleen (enlarged and increased follicles), and, especially in children, a pasty condition in the form of pathological fat formation (Czerny). If status lymphaticus is associated with hyperplasia of the thymus (often to only a

mild degree), it is justifiably spoken of as status thymolymphaticus. Some authors do not separate status lymphaticus from status thymolymphaticus; others, (erroneously see above), consider hyperplasia regularly associated with status lymphaticus (Schridde). In status lymphaticus, or status thymolymphaticus, other frequent associations are hypoplasia of the genitalia, vascular system, especially the aorta, and other congenital irregularities such as lobulated spleen, liver, kidneys, lungs, anomalies of the mesentery, excessively long appendix with funnel shaped proximal part, etc. In view of these various hypoplasias, Bartel placed status thymolymphaticus in close relationship to "a general hypoplastic inferior constitution," the "status hypoplasticus," which perhaps are frequently combined with each other. These individuals are not only especially defenseless against infections (with the exception of tuberculosis, see Weichselbaum) but show remarkable lack of stability of cardiac function and from unimportant occurrences, such as psychic insults, electric influences, minor medical interferences, drop dead from sudden cardiac paralysis (cardiac death). There may be autotoxic influences at work especially from the changed thymus (hyperthymization, Svehla, thymus extract is a hypotonic, lit. by Yokoyama, Hart), but Hammar denies that an altered condition of the thymus produces such results. Ceelen believes a lymphocytic invasion of the myocardium is responsible, (Peacock, Friedjung, lit. J. Bauer). In reference to changes in the blood picture (lymphocytosis), see Borchardt, Hart.

The relation of death during anesthesia and status lymphaticus is frequently pointed out (Gardner, Prevor, and others). Wiesel found hypoplasia of the chromaffin system, especially the medulla of the adrenals in status thymolymphaticus and this has been held responsible for the lowered resistance to external injuries (anesthesia, heat, etc.), and sudden death. This hypoplasia of the chromaffin system would separate more sharply status lymphaticus, or status thymicolymphaticus from status thymicus, in which this system shows no alterations (Hart, lit Adler, lit.), but the changes do not seem to be constant (as for example, the case of M. B. Schmidt). See Hedinger for the frequent combination of status lymphaticus (sometimes with hyperplasia of the thymus) and Addison's disease; he believes a probable mutual cause of both is the hypoplasia of the chromaffin system, especially of the adrenal cortex (Hart, Probst, Kahn, Rossle, v. Werdt; opposed Fahr, Reiche). Others (Kassowitz, Epstein, etc.) view such deaths in children as due to dyspnea or apnea, which is said to develop suddenly in rickets, but also without it. Some deny absolutely the importance of status lymphaticus in these sudden deaths (Richter, lit.), without, however, supplying another more satisfying explanation.

Bartel saw status lymphaticus frequently in young suicides (comp. Pfeiffer, Nost); the author also saw this repeatedly (Miloslavich, lit. opposed Loewenthal).

The results of later anatomical investigations during the war utter a warning against the hasty diagnosis of "status thymolymphaticus." Lit. in appendix.

In leucemia, marked enlargement of the thymus is occasionally seen, especially in acute lymphatic leucemia. The enlarged organ retains its shape; on section it is homogeneous like a leucemic lymph node and is surrounded by a delicate fibrous capsule. But the lymphatic proliferation may also transgress the boundaries of the organ and cause it to fuse with other enlarged lymph nodes.

Hypertrophy of the thymus is very frequent in exophthalmic goiter, under which condition the course of this disease is said to be exceptionally severe. (Lit. in appendix.) According to Hammar, the hyperplasia involves chiefly the cortex, and there is an increase in the number of Hassal's corpuscles, but deviations in the structure of an hyperactive thymus in Basedow's disease may be due to accidental involution. As causes of the hyperplasia, there have been postulated: irritation of the thymus due to hyperthyroidism in exophthalmic goiter (Utterstrom, lit.), but Simmonds found an abnormal thymus in pure thyroidism in only one-half of the cases, while in Basedow's disease over three-quarters showed an abnormal thymus; or Basedow's disease is caused by the combined action of the thymus and thyroid from each of which irritant substances are produced acting on the vagi and sympathetics (Capelle and Bayer); or the thymus hyperplasia and struma are coordinated (Matti), and Basedow's disease with hyperplasia of the thymus is thought to be an unfavorable hyper- or dysfunction of organs physiologically related; or it is due to an ovarian injury caused by the struma which in its turn affects the thymus (Klose, Lampe and Liesegang); or the thymus hyperplasia, free from signs of involution, is a primary and accompanying symptom of a constitutional anomaly representing Basedow's disease with disturbance of the whole endocrine system expressed particularly by struma (Hart). Operative removal of the Basedow thyroid with existing hyperplasia of the thymus is frequently fatal (Nordmann). In some cases without demonstrable participation by the thymus, thyroidectomy in exophthalmic goiter is successful in improving or curing the disease; in other cases, it is necessary to undertake a secondary removal, *i.e.*, reduction of the enlarged thymus, whether clinically manifest or occult. In still other cases of Basedow's disease, the mild thyroid changes do not explain the severity of the symptoms and primary thymectomy is said to be indicated (details by Capelle and Bayer, v. Haberer); other surgeons manage to get

along without thymectomy (comp. *e.g.*, Hildebrand, Sudeck), or they do not consider the results of reduction of the thymus very favorable in exophthalmic goiter.

Hemorrhages in the thymus occur as in other organs, *e.g.*, in the hemorrhagic diatheses; they are said to appear as large as cherries or walnuts in congenital syphilis (Schlesinger); see under blood cysts. Hemorrhages are frequent in suffocated children, usually punctate in size and combined with ecchymoses of heart and lungs (of medico-legal importance!), also in pertussis and other infectious diseases (lit. by Hart). Suppuration, metastatic or by continuity, is rare, but dangerous on account of the accompanying swelling, or possible rupture into the air passages. Pus may collect in the epithelial corpuscles of Hassal (Ribbert). Softened gummas may have a purulent appearance and are observed in syphilitic children, although very rarely. Excessive collections of lymphocytes in the parenchyma resemble abscesses, especially in the large juicy thymus glands of the newborn.

The questions of the etiology and pathogenesis of the abscesses of Dubois in syphilis are much disputed, but most authors now believe they are luetic changes, except Hart, who refused to accept this viewpoint. Eberle and Ribbert believed the cavities were the dilated spaces (originally epithelial) in which pus collections interfered with normal development. According to Chiari, they are due to proliferative invasion into Hassal's corpuscles of thymus tissue undergoing necrosis, while Tuve, Thomsen, etc., see in this the beginning of necrosis of the parenchyma. Simmonds described invasion of Hassal's corpuscles, principally by lymphocytes, eventually with leucocytes (Schridde speaks only of the latter) which lie in irregular cavities surrounded by epithelial proliferations derived from adjacent tissue. Simmonds also found spirochetae pallida in the contents of the cysts. Hammar (lit. to 1918) considers them sequestrum cysts, *i.e.*, after luetic necrosis of the parenchyma (sequestrae, see above); the lymphocytes are secondary invaders and surrounding reticulum cells arrange themselves into an epithelial lining for the cyst. By solution of the corpuscular elements of the cyst contents there develop the so-called Bednar's cysts containing yellow serum. Hemorrhages into these cysts produce blood cysts. In all cases of congenital lues, Hammar found in addition, marked invasion of lymphocytes into Hassal's corpuscles, but such invasion is not rare in normal thymus glands. According to Hammar, sequestrum cysts of considerable dimensions have thus far been observed in man only in congenital syphilis, (lit. by Herxheimer and Hart). See Fulci in reference to the experimental production of alleged analogous structures. Haerle saw small necroses, containing spirochetae with abscesses, in other organs in congenital lues (lungs, tonsils, ileum).

Tuberculosis is almost always secondary as miliary tubercles or caseous nodules. Hart considers the disease infrequent.

Tumors are quite rare. As points of origin of malignant tumors must be considered: 1, epithelium of the medulla and Hassal's bodies; 2, the small cortical cells; 3, interlobular connective tissue. Those derived from the former are carcinomas (lit. Lange, Stockert, Rubaschow, Robbers, Schmittmann); those from the second, if we share the opinion that they are lymphocytes or round cells, or at least lymphoid structures, are lymphosarcomas, but since this is still a disputed question, Simmonds suggests the name "thymoma" (Grandhomme). But with Schridde, Hart and others, the author cannot call this designation satisfactory; it would perhaps be better to call them malignant thymus tumors as Schridde does, who, however, believes in their epithelial nature. Tumors with uniform, small, round cells, devoid of reticulum (as in lymphosarcomas) and containing neither Hassal's corpuscles nor remannts of the thymus gland, as in many mediastinal tumors which typically cover the heart like a cap, may perfectly well be called round cell sarcomas. Simmonds described two sarcomas derived from (3) connective tissue (spindle cell sarcomas), see Brand. Other literature by Wiesel, Brandt, Nicol. Lymphosarcomas of the thymus in contradistinction to nodular lymphosarcomas from mediastinal lymph nodes are diffuse growths, as a rule, with smooth, homogeneous section surfaces (p. 278); they may contain Hassal's corpuscles, which is of diagnostic importance (Letulle; Delesseret). Leucemic tumors (see above) of the thymus, not rare during childhood (Benjamin and Sluka), may cause difficulties in diagnosis, for without blood counts, they may be mistaken for sarcomas or lymphosarcomas. In chloroma also (p. 272), tumors of the thymus sometimes occur, but, on the other hand, practically never in pseudoleucemia or lymphogranulomatosis. Combinations of dermoids and lymphosarcoma also occur.

See Lange, Yamanoi for rare lipomas of the thymus.

Neoplasms of the thymus have been repeatedly observed in myasthenia gravis (see p. 542 and under spinal cord). There is a tendency to assume a correlation in the nature of a toxemia of unknown origin, (lit. Mandlebaum Celler).

Congenital Cysts. Teratomas. Ciliated epithelial cysts have been encountered in the anterior mediastinum; the tracheal diverticulae mentioned above (H. Chiari), or congenital displacements and snared off particles from the bronchial tree (Stilling, Zahn), have been held responsible (also congenital pulmonary adenomas, Linser), but, on the other hand, the entodermal epithelium of the primordial thymus, capable of differentiation, may also be a point of origin. This probably also holds good (Marchand, Schridde) for some dermoid cysts, usually lobulated, multilocular

tumors with yellow white, fatty or mortar-like, poultaceous contents including hair, but they may arise from inclusions of epidermis during the closing of the thorax. Cystic teratomas appear similarly, but contain cartilage, bone, mucosa, or tissue from all three germinal layers (see the observation of the author, reported by E. Hornicke in a soldier 25 years old); genetically, these have nothing in common with the thymus (Ekehorn, lit.). Usually they are small, but may be very large (Virchow), and force themselves into the pleural cavity. Solid mediastinal teratomas (Lindstedt, lit.) very rarely reach the size of a man's head (Sieber, lit.). Combinations of dermoid cysts and lymphosarcomas also occur. See Ceelen for carcinomatous change in a cystic teratoma; and Stein, carcinomatous and sarcomatous transformation of a solid teratoma, (Prym, Pohl, lit.). The designations, "cystic dermoids" and "cystic teratomas," are used quite promiscuously.

Tumors of the thymus are clinically called "mediastinal tumors," which may include tumors of bronchial and mediastinal lymph nodes, *i.e.*, primary aleucemic lymphomas (also lymphogranulomatosis. Oestreich, Nicol, Tuchmann), lymphosarcomas and ordinary sarcomas (see above, and Hebert), or secondary tumors such as bronchial carcinomas or lipomas and lipogenous sarcomas (Koster), diffuse lymphangiomas (Schmincke, etc. All these tumors become dangerous from pressure, invasion of surroundings (air channels, vessels, esophagus, nerves, heart, etc.).

The clinical differential diagnosis also considers aneurysms of the ascending aorta, the innominate or subclavian arteries, echinococcus cysts, abscesses in the anterior mediastinum, substernal goiters, etc., (Schinz, lit.). [Phillips, J., J. A. M. A. 78: 1355: 1922. For thymic tumors, see also Brannan, D., Arch. Path. & Lab. Med., 1, 569, 1926. Foote, N. C., Am. J. Path., 2, 33, 1926. Brown, S. E., Arch. Path: & Lab. Med., 2, 822, 1926.—*Translator.*]

## Thyroid Gland

**Anatomy** (see Sobotta).- The thyroid gland (Wharton) has no excretory duct; it consists of two lobes on either side of the larynx connected by a glandular bridge, the isthmus, which crosses the trachea at the level of the second and third cartilaginous rings. It has a fibrous capsule surrounding it externally; internally there are trabeculae which divide the organ into lobules; smaller connective tissue bands form the alveolar and follicular septa. The follicles are closed cavities formed by secretion into a rounded epithelial mass; the lining is of epithelial cells, cubical to flat, more rarely cylindrical, and not clearly separated from each other; there is no membrana propria, at least not under normal conditions (see Wegelin). The secretion contained in the cavities is an albuminous sub-

stance, "colloid", present in greater or less quantity. In fetal life, the gland becomes typical in the fourth month, but immediately after birth there is marked cell desquamation and no colloid. According to Boye, this desquamation and cessation of colloid secretion begins in the seventh to eighth month in utero; but by regeneration, it recovers its normal appearance in the next weeks, (see Elkes, Hesselberg, lit., Sumita, Gleim, Staemmler). The colloid is formed in the cell protoplasm from acidophilic granules or fine droplets which, when expelled into the alveolar lumen, coalesce into a homogeneous, gradually thickening, colloid. This takes a bright red color with eosin; by van Gieson's method it stains yellow to brown. (See details by Krause, who distinguishes two normal forms of secretions, one tannic acid fast, and one fuchsinophile.) Here and there in the colloid are a few red and white blood cells, as well as frequent droplets of lighter staining material which can be noted at the edge of the homogeneous mass filling the space. In the epithelium are present small fat droplets even in the newborn and increasing with age, a so-called wear and tear pigment, perhaps a decomposition product of fat-like bodies (see Hueck) and doubly refracting lipoid substances (see Haeberli). Damberg speaks of glycogen in the thyroid. The alveoli are surrounded by numerous blood capillaries. A network of lymph vessels lies in the supporting structures; they may contain colloid although Lubcke believes the substance is coagulated blood or lymph plasma (see Sarbach for the opposite). The secretion becomes thicker and thicker and can probably not be absorbed but it does supply the organism with active substances, perhaps by diffusion or absorption into the surrounding blood capillaries (see also Ebner). Direct entrance into lymph channels through open spaces in the epithelial wall (Langendorf and others) or through intercellular channels (Hurthle) is very doubtful according to E. Schmidt, Isenschmidt, and others, but is possible in animals (Matsunaga, see also O. Ewald). At many of their bifurcations, the smaller arteries have a sort of thickening of the intima, the so-called cell-buds (M. B. Schmidt) which consist of elongated cells, probably muscular, with the supposed function of closing apparatus (see also Sanderson-Damberg, lit.). There are many larger and smaller nerves which penetrate the gland substance. The thyroid glands in goiter-free territories are distinguished from those of territory with endemic goiter by their larger vesicles and greater colloid content. With age the follicles become smaller, the epithelium swells, the nuclei become abnormally large, are lighter or darker, fat-containing pigment is more plentiful, the colloid hardens, and the arteries show calcification of the intima (see Clerk). In goiter areas such as Bern, the thyroids are nearly twice as large as in the north of Germany, and they show great increase in connective tissue. The size of the thyroid changes in different localities. It is

smaller in the north of Germany than in the south. In goiter regions, it has a greater weight, and in Switzerland more than $^5/_6$ of all inhabitants have thyroids exceeding the heaviest weight of those in goiter-free regions (see Oswald). For the physiology of the thyroid gland, see under cachexia thyreopriva, pp. 527–528.

**Embryology. Malformations.**—The thyroid gland, derived from the entoderm, develops from two lateral anlage which grow from the fifth (the last) branchial cleft, and from one median anlage. The lateral anlage can hardly be considered in the formation of the main bulk of the organ,

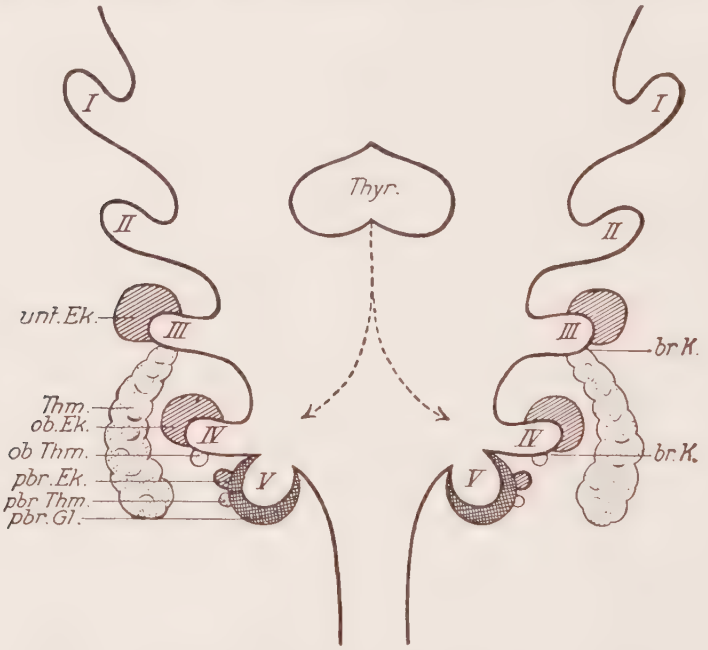



Fig. 219.—Branchial derivatives diagramatic (after Getzowa, V.A.,2 05, 1911). Thyr, thyroid gland; arrows indicate direction of growth; I to V gill clefts. EK, parathyroid bodies; unt. ob. pbr., lower, upper, postbranchial; Thm, main thymus; pbr, post branchial thymus tissue; ob, upper thymus metamere IV, pbr. gl., postbranchial gland or body (shaded crosswise).

although according to some, they form thyroid gland tissue which blends with the median anlage (Erdheim). They may, however, eventually be the starting points of malignant goiters (see p. 533). Such things as cyst formation, solid heaps of large cells, other heaps with small lumena in the atrophic thyroids of cretins and idiots, and in thyroid aplasias (see Dieterle, lit.), are related to the post branchial bodies (Kursteiner, Getzowa), but some consider them indifferent remains of branchial ducts (Erdheim, Zuckermann, Schilder). To follow Broman, the median anlage begins as a solid epithelial protuberance on the anterior pharyngeal wall in the median space between the ends of the 2nd gill clefts; it then grows down-

ward, stopping at the cranial end of the trachea to form the main body of the thyroid, from which the two lobes develop, each with a lumen. At the same time (middle of the 4th embryonal week), the cranial part of this epithelial growth, the so-called ductus thyreo-glossus, receives two lumena. The duct then becomes elongated and atrophies, usually at the end of the 4th week, remaining only as a connective tissue cord, the tractus thyreo-glossus. According to others, the thyroid anlage separates from the pharynx as a pedunculated vesicle. The patent stem of this vesicle is the ductus thyreo-glossus, and the two-lobed anlage with their divided lumena which were formed before the separation, lose these, when separation of the duct takes place. The two-lobed anlage grows into a broad body consisting principally of transverse cell columns. The derivatives of the caudal branchial complex arrange themselves laterally, becoming partly surrounded, chiefly the post branchial body which loses its lumen during the process (see Grosser). The duct often remains partially preserved at its starting point in the buccal cavity as the so-called foramen coecum of the tongue. Occasionally, 2.5 cm. of the duct persists (ductus lingualis) and can be traced from the foramen coecum to the hyoid bone which encloses the duct remains. When the caudal part of the thyreo-glossal duct does not disappear, it is usually transformed into the glandular tissue of the so-called pyramidal lobe, a prolongation extending from the thyroid isthmus upward, or it is snared off as a median parathyroid suspended from a tube which extends to the hyoid bone. The epithelium of the median thyroid anlage forms a series of sprouts soon becoming tubes, separated by connective tissue. These epithelial tubules are later beaded or chain-like, and finally separate into numerous epithelial vesicles surrounded by vascular connective tissue. Cysts, fistulae and solid tumors related to the entodermal thyreo-glossal duct (see also p. 328, and under mouth cavity, p. 575) originate either (*a*) from a section of the lingual duct, or, more rarely, from the thyreo-glossal duct which remained patulous throughout its whole length (Matti, lit.), or (*b*) from efferent tubules of cylindrical epithelium accompanying the duct (M. B. Schmidt). The first (*a*), lined with ciliated epithelium, or with pavement epithelium in layers, are found in the neck as median cysts, with external fistulae if the skin is perforated. They may extend to the hyoid bone, or to the apex of the pyramidal process (Streckeisen). Parathyroids similarly formed from rests of epithelial tubules, often are present somewhere along its length. The others, (*b*), are secondary to budding along the lingual duct which persists at the lingual end. They are mostly mucous glands, to a less number, tubular channels of cylindrical epithelium (Bochdalek's ducts), (lit. by Erdheim, Berard et Chalier, Schilder). Ranulas develop from cystic dilatation of these structures (see p. 574). According to Dieterle, all of these forma-

tions can be related to the salivary gland of Vater, a convolution of rudimentary salivary glands, corresponding to the ductus thyreo-glossus of His; it has no relation to the thyroid gland. There is nothing analogous known in animals (Schaffer), and the reports of Grosser, among others, refute this idea in the human embryo as well.

Absence of parts of the thyroid gland is observed occasionally; complete aplasia occurs in rare instances, thyreo-aplasia or athyreosis (see p. 526). In the latter instances, growths on the base of the tongue composed of thyreo-glossal duct structures showed derivatives of pavement and ciliated epithelium and thyroid tissue.

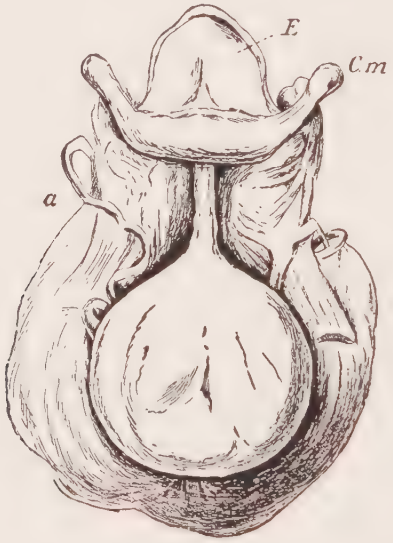



FIG. 220.—Struma of the snared off pyramidal process of the thyroid gland adherent to the posterior surface of the hyoid bone and suspended free to the isthmus, but without any relation to it. The snared off, strumous process, pyr., is supplied by a branch of the superior thyroid artery (a); both lateral lobes enlarged; E, epiglottis; Cm, large cornu of hyoid. 61 year old woman.

Accessory thyroids are not rare; they may be scattered over wide areas, such as behind the sternum to the arch of the aorta, upward to the base of the tongue, laterally to the confines of the large vessels of the neck, etc., (see p. 510). They have been found even in the inner larynx and trachea (Heise, R. Paltauf, etc., Enderlen, lit.). The author saw an intratracheal colloid goiter the size of a cherry stone in a man 67 years old. These misplaced accessory thyroids may become pathologically enlarged, and thus offer diagnostic puzzles in the living (pp. 323 and 564).

**Circulatory Disturbances. Inflammations.**—Passive hyperemia is observed in cardiac lesions and compression of the veins of the neck, *e.g.*, from tight collars. It causes swelling, and perhaps favors goiter formation.

Experimentally, Luthi saw changes somewhat resembling thyroiditis simplex, but the formation of new epithelium and leucocytic invasion were absent.

Active hypermia and probably parenchymatous swelling also, are often coincident with menstrual or pregnancy hypertrophies.

See B. Beck, Rubsamen (lit.), Muller, in reference to thyroid swelling and goiter during pregnancy. Perhaps ovarian hormones play a role (see F. Cohn).

Wanner saw increased thyroid secretion in animals when anemia was repeatedly produced.

The author saw fat emboli in the capillaries of the thyroid after fractures.

Inflammation, thyreoiditis, is rather rare, at least to massive macroscopic degrees. But abscess formation occurs from local wound infection, or by metastasis, as in malignant endocarditis, typhoid fever, pyemia, etc., or by continuity as in diphtheria, and from degenerating laryngeal tumors.

Occasionally, the gland shows innumerable miliary abscesses, as in septic abortion. Larger abscesses are rare.

De Quervain and his pupils (Sarbach, Aeschbacher) frequently observed non-suppurative inflammations — thyreoditis simplex — recognized by hyperemia, fluidity and disappearance of colloid, presence of foreign body giant cells, hypertrophy and desquamation of epithelium, leucocytic and round cell infiltration into vesicles and occasionally interstitial proliferation, after destruction of thyroid tissue (fibrous atrophy —Simmonds), especially in chronic pulmonary tuberculosis (see Sarbach). The iodin content decreases, and this may lead to thyreosis, to hypo- (see Bayon), but also to hyperthyreosis (see under Basedow's disease, p. 516, and see Hollos, probable role of tuberculosis). In children the changes are usually slight (Thomas, lit.). Leucocytes and interstitial proliferation are absent in intoxications, but there is acute swelling, *e.g.*, after the use of potassium iodide (toxic thyreoiditis, or toxic reaction, de Quervain, see Sellei).

In a case of purpura neonatorum, Pettavel found peculiar focal degenerations in the thyroid epithelium.

Simple exudative (parenchymatous) and purulent inflammations are somewhat more frequent in goiter and the acute swelling is sometimes sufficient to kill by suffocation. Fatalities by the same route have occurred in abscesses.

Abscesses may perforate into the trachea, but they also heal by fibrosis and calcification. Types which form sequestra are also known; they might be called strumitis dissecans. The author saw this in facial erysipelas.

Chronic indurative inflammation may cause stony hardness (see Silatschek), occasionally mistaken for a malignant neoplasm (O. Meyer, lit.; Brunger, combination with Basedow's disease).

Hashimoto considers the so-called struma lymphomatosa a peculiar type of chronic inflammation; it is characterized by enormous overgrowth of the lymphatic elements, especially the lymph follicles, and by certain parenchymatous and interstitial changes of remarkable firmness. The condition is prognostically favorable.

**Enlargement of the Thyroid Gland, Struma or Goiter.**—By struma or goiter is understood an enlargement of the thyroid gland. (The term "struma" is also used in connection with the adrenal and pituitary glands.) Enlargements appear in malignant growths, carcinoma or sarcoma,—benign growths, transitory in arterial or venous dilatation, and benign hypertrophic processes, diffuse or nodular, localized to parts, a side, or to the isthmus alone. A movable lobe springing from the isthmus may be found suprasternally, or in the upper thoracic aperture, or underneath the sternum (divided goiter); the whole thyroid gland may be forced downwards, and a detached part lies under the sternum in the neighborhood of the arch of the aorta (substernal goiter). Or, a prolongation descends between the trachea and esophagus, and if it becomes goitrous, may cause severe discomfort. The author saw such a tumor exceeding the size of a fist. Circular goiters (Wolfler) surround the trachea and esophagus and may extend backward between the posterior wall of the esophagus and the spinal column (rare). Retrovisceral goiters are also rare, (C. Kaufmann), and may be differentiated into isolated and retrovisceral accessory goiters (Wolfler). Payr and Martina separate the accessory goiters into two groups according to their starting points: (*A*) from the middle, or (*B*) from the lateral thyroid lobes. They divide (*A*) into (1) superior (lingual, hyoideal), (2) inferior (retrosternal, intrathoracic), (3) anterior; and (*B*) into (1) posterior (retropharyngeal, retroesophageal), (2) lateral (submaxillary, lateral, retroclavicular), (3) those in the respiratory tract, (intralaryngeal, tracheal, bronchial). Intrathoracic goiters occasionally simulate pulmonary tumors (see K. Mayer), or aneurysm of the aorta, or mediastinal tumors displacing lungs and heart.

A diffuse enlargement is the essential characteristic of the endemic goiter. The goiter of Basedow's disease will be discussed later. Nodular goiter, *i.e.*, thyroid enlargement from circumscribed nodules within the gland, is entirely different. The nodules are adenomas and do not depend on endemic conditions, but occur everywhere. Diffuse enlargement and nodule formation are often combined.

In the diffuse (1) and the nodular goiter (2), (*a*) parenchymatous, and (*b*) colloid or gelatinous types may be differentiated.

(1-*a*) The enlargement of the diffuse parenchymatous goiter (follicularis) is caused by numerical hyperplasia, *i.e.*, new gland parenchyma. The exuberant gland epithelium forms solid globular, or ovoid cell heaps or columns, and rounded or elongated vesicles and branching tubes. Some vesicles contain colloid. The tissue is fairly firm, fleshy, brownish red, or with less blood content, gray. The size, according to de Quervain, never exceeds three times normal, and the horse-shoe shape of the thyroid remains as before. To differentiate the histological picture of Basedow's disease which is also a diffuse parenchymatous change, see page 516.

FIG. 221.—Parenchymatous (adenomatous) goiter. From a small yellow nodule; glandular, rounded and elongated branching structures, seen partly from the surface (medium magn.).

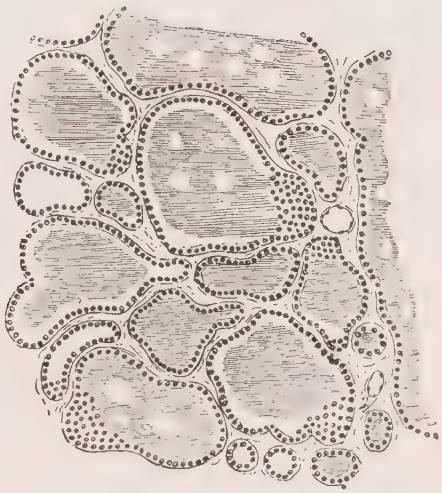


FIG. 222.—Colloid goiter; smaller and larger gland vesicles filled with colloid; stained with carmine and picric acid (medium magn.).

(1-*b*) In the diffuse colloid or gelatinous goiter, the newly formed acini are completely filled with colloid and stretched to several times their normal diameter. The lobulation is usually obscured. Naturally, the enlargement is much greater than in (1-*a*), and there is a controversy concerning whether there is hyperemia with hypersecretion (Hellwich) or retention from insufficient absorption—colloid stasis, (Rautmann). According to Oswald, colloid goiters, in direct opposition to Basedow's goiters, are accompanied by a hypothyreosis. The multiplication of acini results in pressure which causes more or less flattening of the epithelium. The colloid is sometimes less viscid than normal, often somewhat granular, but many times, of the consistency of normal colloid; it is usually somewhat transparent, may be more or less firm, like boiled sago, or even rubber, yellowish brown, red, or deep brown in color. The complexes appear like fish roe, and resemble cross sections of a filled honeycomb.

Clumps may reach the size of peas or of cherries or even larger. Disappearance of the partitions leaves large colloid cysts by confluence—cystic colloid goiter. These are often of large size with smooth globular or nodular surfaces and perhaps with fibrous induration. A diffuse colloid goiter may contain colloid adenomata enclosed in actual capsules and sharply separated from the surroundings.

Colloid is also found in the interstitial tissue, and in lymph vessels; according to Monogenow, it is especially abundant in nodular goiter.

(1-*c*) Diffuse vascular goiter is characterized by many dilated arteries and veins in a simple—or a colloid diffuse goiter (vessel goiter).

On the other hand, this type includes those enlargements which depend exclusively on a temporary or permanent dilatation of arteries and veins;

FIG. 223.—Nodular colloid cystic goiter. L, trachea covered anteriorly by thyroid, compressed laterally; h, membranous posterior portion of trachea, esophagus behind. Colloid masses of various tints from yellow to brown. Horizontal section; $^{9}/_{10}$ nat. size.

in such a case it is spoken of as transitory struma hyperemia, or aneurysmal or varicose struma.

Vascular goiters may grow to immense size; sometimes they appear in young individuals. Congenital goiters (see p. 523) are often vascular, but in other cases, parenchymatous.

**Circumscribed Goiter—Nodular, Adenomatous Goiter.**—Sharply demarkated nodules appear in the thyroid, surrounded by a fibrous capsule; they can be shelled out easily and are very variable in number, size and appearance. Adenomas, *i.e.*, glandular tumors, are either parenchymatous, soft, opaque, white to brown, or are completely, or partially colloid in make up. Their appearance is further modified by various regressive changes such as fatty degeneration, hemorrhage, cyst formation, etc., (see p. 520).

Their number and size usually increase with age, beginning at the time of puberty. They do not occur in children. Occasionally but a single nodule is found, but in other cases, a lobe, or the whole thyroid is filled

with numerous tumors, often colloid, and not rarely cystic. The thyroid tissue between them is compressed and partly fibrosed (see deCoulon), or present as a coincident parenchymatous or colloid goiter. Such irregularly formed and eventually very large, nodular glands are quite frequent in goiter regions (influence of goiter noxa?, see Th. Kocher), although adenomas are by no means rare in goiter-free, low plain countries where, however, they remain small, as a rule, *i.e.*, cause no remarkable enlargement or goiter (see Kloeppel).

Opinions differ as to their point of origin. Wolfler, in reference to the form he calls fetal adenoma, usually developed as multiple growths at the time of puberty, especially in the peripheral parts of the thyroid, attributes the origin to the growth of embryonal cell rests lying between the follicles. But proof is wanting of progressive development of these rests into nodules, and the possibility is not excluded that these insufficiently characterized groups of cells are, in reality, parathyroid brancheogenic inclusions which are better known today, or merely true lymph nodules. For this reason, Wolfler's theory has not been accepted by Hitzig, nor by Michaud, (see also Vogel and others), who demonstrated development nodules from the epithelium of the acini which changed its character. The tubules are contrasted from the surrounding tissue by their diameter, their branching, and prolongations, their high cylindrical epithelium, more intensive nuclear staining and, in the early state, by their richly cellular structure. Ribbert, in his turn, rejected Michaud's theory of post fetal sprouting, and demonstrated inclusions of germinal tissue, presumably embryonal, which differed from the uncertain cell rests of Wolfler by having characteristic solid epithelial masses; these are the points of origin of adenomata.

**Goiters with Embryonal Gland Structure.**—Langhans rejects the designation of Wolfler, "fetal adenoma," since it does not specify which developmental state is present, viz., that of solid cell masses, of cell columns and tubes, of cell clumps, or of actual acini; on the other hand, Langhans reports rare forms which he considers related to developmental inhibition. Fig. 224 illustrates such a case; the picture is repeated in innumerable nodules. A network of connected cell strands lies in a homogeneous stroma, poor in nuclei. Some of the cell strands are changed into rounded acini, but their arrangement in rows, and the failure of most to reach the stage of individual acini speak for a delayed growth. The author would like to call these formations which suggest a string of beads (see p. 507), "vesicle strands" or "vesicle strings."

**Translator's Remarks.**—It is quite possible to use a classification of goiter which combines anatomic with physiological considera-

tions, not that it is always possible to correlate anatomy with physiology nor physiology with anatomy in a goiter, but such a classification at least has a dynamic ring, and serves to keep alive in the minds of both the pathologist and the clinician the idea that the thyroid gland is a labile organ and that there is no one picture which is normal, but that many are so. As emphasized in the text, what is normal for the gland in a non-goitrous region may not be normal in a goitrous region such as in Cleve-

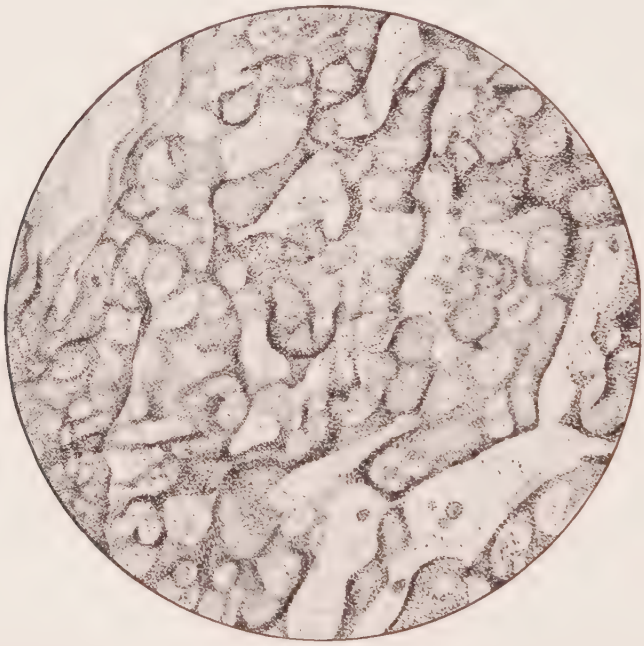


FIG. 224.—Goiter with embryonal form of glandular constituents. Net-like vesicular rings, reticulated homogenous lighter stroma, poor in nuclei. (After Langhans, V.A. 206, 1911.)

land or in Switzerland and vice versa. The thyroid also, as stated, undergoes changes at puberty, at menstruation, at conception, during pregnancy and at the menopause, these changes varying in degree according to the individual, *i.e.*, according to the individual's physiological needs. There is probably also a seasonal variation in the activity of the gland, a temperamental, etc., all of which are probably reflected in its appearance. With these things in mind we may classify a thyroid gland as a goiter when it is in excess of a certain weight, depending largely on the region in which the individual lives, *e.g.*, 40 grams around Philadelphia, 60 grams around the Great Lakes. When there is an increased demand for function the first changes manifest are

hypertrophy of the lining cells, that is, a change from cuboidal to cylindrical, and then a hyperplasia, *i.e.*, increase in their number. With hypertrophy and hyperplasia there is a diminution in the size of the vesicle and thus a diminution in the amount of colloid present irrespective of the balance between production and absorption, which of course determines also to a large extent the amount of colloid present in a gland at the time it is examined. Such an hyperplasia and hypertrophy may then disappear and a practically normal gland remain, or what is more likely, the spaces become larger and irregular in size and contain a larger amount of colloid. The lining cells are then again cuboidal. Another possibility is that the hyperplasia and hypertrophy continue until the gland is "worn out," whereupon atrophy supervenes. The colloid gland may remain as such, or once more undergo hypertrophy and hyperplasia to lead to a still larger colloid gland or perhaps one of the same size, or to atrophy, and so the cycle may be repeated. A further important consideration is that the so-called adenomas undergo the same changes; in fact, physiologically, the secretion in adenomas, as far as experiments to date are concerned, if not exactly the same, is at least not very different in its effects from that of the normal gland; we may have hypertrophy, hyperplasia, atrophy and colloid stage in an adenoma. According to these considerations, we might classify goiters, *i.e.*, enlargements of the thyroid, as

(1) stage of hypertrophy
(2) stage of hypertrophy and hyperplasia
(3) colloid stage

and adenomas in exactly the same way.

Viewed from this angle, it is not difficult to believe that the so-called fetal adenoma is thyroid adenoma tissue not yet undergone the proper amount of hypertrophy and hyperplasia and formation of colloid.

Furthermore it is quite possible to classify the colloid stage as the resting stage.

In the discussion below it is stated that the symptoms of exophthalmic goiter may be present when the gland is in the colloid stage. In the translator's experience, this is true in from 25% to 30% of the cases, this statement to be modified by the fact that the majority of glands examined were operative specimens in which the entire gland was, of course, not examined. From autopsy experience, the translator has found that these hyper-

trophy, hyperplasia, colloid, atrophy, etc., stages may be all present coincidently in one and the same gland so that examination of a small portion may show one picture and examination of another portion, another. Coupled with the well-known tendency of goiters and adenomas to undergo various degenerative changes, it makes for apparently extremely complicated pictures but when viewed in the light of the above thoughts, the difficulties disappear and classification is rendered fairly easy.

Below are also discussed various physiological considerations concerning Basedow's disease. Enough is said, but the opportunity cannot be passed of protesting against the clinical division of exophthalmic goiter and toxic adenoma into two distinct diseases. According to the translator's experience, in a goitrous district for several years, but later in a non-goitrous district when the experience was small but nevertheless definite, the symptoms of exophthalmic goiter may be present when adenomas are also present, and vice versa, but for a good discussion of this subject with which the translator heartily concurs, see Graham, A., J. A. M. A., 87: 628, 1926; and Ann. Surg., 84: 497, 1926. For the physiology of the thyroid gland, see Marine, D., Physiol. Rev., 2: 521, 1922 and work by Marine and collaborators since that time. For the pathological anatomy of the human thyroid gland, see Marine, D. and Lenhart, C. H., Arch. Int. Med., 7: 506, 1911. For exophthalmic goiter, see Arch. Int. Med., 8: 265, 1911. For critique of the surgical treatment and other opinions in regard to the thyroid gland, especially the question of the rationale of removing part of a gland which is compensating to supply a bodily need, see Hoover, C. F., "Does Hyperplasia Offer Any Evidence for Thyreogenesis of Graves' Disease?" Am. J. M. Sc., 173: 11, 1927. For interesting data on thyroxin, its preparation, synthesis and differences in various countries and during various seasons, see paper and references of Kendall, E. C., J. Biol. Chem., 72: 213, 1927. For relationship between histological structure and biological activity of goiter tissue, see DeQuervain, F., Surg., Gyn. and Obst., 513, 1922.

**The Diffuse Goiter of Basedow's Disease** (named after v. Basedow, a physician of Meroeburg—1840).—This is a juicy, parenchymatous goiter which eventually exhibits pulsation and vessel bruit. Among the symptoms is exophthalmus, which is inconstant, sometimes unilateral, and due, it is thought, to irritation of thus far unknown smooth muscle fibers, musculus orbitalis in the bulb (for this and other explanations, see

Landstrom, Worms and Hamant, lit.). There are also accelerated pulse rate, and palpitation and dilatation of the heart (see thyreotoxic goiter heart, p. 523). The symptoms of Basedow's disease (Grave's disease) appear mostly in early middle life. The disease is more frequent in women, and is considered a hyperthyreosis, a secretory exacerbation, but, according to others, is due alone, or is coincident with dysthyreosis, *i.e.*, a pathologically disturbed function of the gland (E. J. Kraus, Ribbert). According to Oswald, it has not been proved that the thyroid gland is the prime instigator of Basedow's disease; he thinks a primary "weakening" or exhaustion of the nervous system is of deciding importance. Melchior believes that Basedow's disease is a pluriglandular affair, the expression of a general constitutional anomaly, and the severity of this basic disease is also chiefly responsible for post operative Basedow deaths. According to Koeher, there is an increase, greater fluidity and higher iodine percentage of the secretion; enlargement, and increase of cells go hand in hand with increased vascularization. The demonstration of increased absorption of iodine, a substance derived from the air and the food and used by the thyroid in the manufacture of its secretion, makes it possible that Basedow's disease is related to overproduction of an excretory product which overwhelms the organism. In this connection, it is interesting to note that even the sparing use of iodine, which often favorably influences goiter, sometimes causes symptoms suggestive of Basedow's disease, but, according to Oswald, only in certain, already pathological, individuals (iodine Basedow's, Th. Kocher). Doubtless the iodine received and taken up by the thyroid, stimulates the formation of some substance which is secreted in such quantity or quality as to cause Basedow symptoms. On normal men and animals, thyroid juice acts the same as the juice of goiters, (Baruch)—according to Klose, only that from Basedow goiters. Exophthalmic goiter also follows an acute thyreoiditis (DeQuervain, lit.). O. Bardenhewer denies that Basedow's disease is identical with iodine poisoning, (Klose and others). Kocher and Nolen mention an almost constant swelling of regional lymph nodes as consequences of the irritation of a functionally changed thyroid. See p. 501 in reference to the frequent thymus hyperplasia in Basedow's disease. E. Bircher, by implanting thymus into dogs, created the complete symptom complex of Basedow's disease. Klose achieved the same result with juice pressed from Basedow thyroids, but it is important to remember that he used dogs degenerated by close inbreeding (see Oswald). Rational treatment requires first of all a reduction of thyroid mass by operation or x-rays, or antitoxic medication, *e.g.*, milk of thyroidectomized goats (see p. 501 as to operative treatment and Th. Kocher's remarks; also Bing, Sattler, Cohen, Hollos, Klose, Chvostek, Hofstatter in relation to treatment). The blood findings by

Caro, von Lier and by Turin, who considered the lymphocytosis and neutrophilic leukopenia as characteristic of Basedow's disease, are disputed by C. Muller, Bauer and Hinteregger, Blank, etc., who recognize no characteristic Basedow blood picture.

The enlargement of the thyroid is usually diffuse; nodules are found only in a small proportion of cases. Macroscopically, the appearance differs, but as Kocher says, the characteristic picture of a true Basedow thyroid is that of a diffuse parenchymatous goiter, which is compact, finely lobulated, and rather pale; the vascular abundance is recognized only after injection; it is more or less opaque, soft, or only moderately

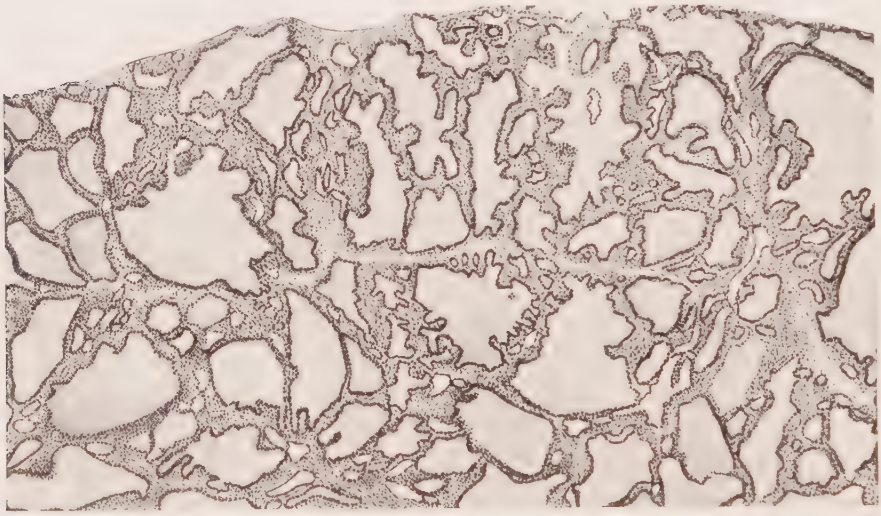


FIG. 225.—Goiter in Basedow's disease. Folded, papillary, high cell foci (Basedow foci) in a colloid goiter; the latter with low epithelium, alveoli with smooth walls (especially extreme left of picture); woman 27 years old; (low power).

firm, and from the section surface a watery juice may be scraped by the knife. At other times, however, it resembles a colloid goiter. A general description of the microscopic findings is also quite difficult, because Basedow changes may establish themselves in an already formed, purely diffuse hyperplastic goiter or vascular goiter (Th. Kocher; lit. of histology, see appendix). In an otherwise ordinary goiter, the more or less characteristic changes of Basedow may often be seen only in isolated foci. And as Haemig emphasized, certain cases of Basedow's disease display the microscopic picture of common colloid goiter. The author saw this 3 times in 26 cases. Pettavel saw it with common parenchymatous goiter. The pathological anatomy is therefore not always characteristic, (see also Simmonds, Matti). When this is the case, however, the following microscopic changes are usually found.

1. Changes in the content of the acini: the colloid is thin, stains faintly with eosin, the old material is liquefied, that freshly produced remains thin (easily absorbed), sometimes it is only a loose coagulum; the old contains much iodine, but the later fluid is poor in this substance (A. Kocher). Changes in the epithelium: (*a*) cells become higher, cylindrical, and are more sharply separated from each other than usual; (*b*) increase in number is shown by folds and papillae, giving the alveoli a polymorphous or adenomatous appearance. Such areas may, however, appear here and there in colloid goiters. In addition to enlargement, there is branching of tubules

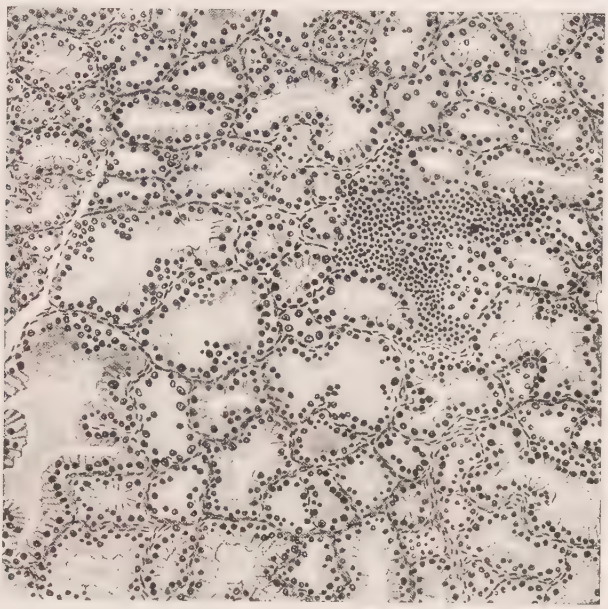


FIG. 226.—Goiter in Basedow's disease; narrow alveoli, high cells, in places polymorphous and desquamated here and there; thin floccular colloid; lymphoid tissue focus in interstitial tissue (high power).

and an increase in acini; (*c*) according to A. Kocher, severe, fatal cases may show irregular hyperplasia and multiplicity of layers, not of cylindrical, but of polymorphous cells with polymorphous nuclei. The acinar contents also show desquamated cells. According to Kocher, (*a*) and (*c*) frequently combine. At any rate, the author has observed (*a*) more frequently, and found it far more characteristic. Much attention is given to the presence of lymphoid tissue (Farner), or true lymph follicles, even with germinal centers in the interstitial tissue (Langhans). Statements vary as to their frequency. They occur, although rarely, in common goiter and even in non-goitrous thyroid glands. They are absent in children. Simmonds found them in 80% of Basedow goiters, A. Kocher in 83%. Others found them rarely. The author saw them 8 times in 28 Basedow

cases. Whether they are the result of some stimulation due to the inactivity of the adrenal system (Dubois), or of dysthreosis (Simmonds), or vice versa, or are proof of the inflammatory nature of Basedow's disease (Brunger), is undecided. In cured cases, the colloid thickens, and cellular changes regress.

Basedow symptoms have been but rarely observed in thyroid neoplasms with colloid-producing metastases (Ehrhardt, Loewy), or in tumor metastases in the thyroid (Mori, lit.). v. Taksch and Rotky mention bone changes of an osteomalacia-like type. Parisot discusses the occasional glycosuria in this disease. Th. Kocher mentions improvement during pregnancy, and Huebschmann reports on the remarkable shortness of the small intestine.

Thymus hyperplasia is usually moderate, but quite often present; according to A. Kocher, it weighs 15 to 30 gms., rarely above 50 gm., and occurs in over 70% of the cases (for details see Hammar, p. 501, also for operative treatment). The adrenals are said to show cellular hypertrophy with hypoplastic medulla, (among others, see Pettavel). For the relation of the hypophysis and Basedow's disease, see Hofstatter; Rautmann, (collected lit.), for the condition of all organ systems in Basedow's disease.

**Further Changes in Goitrous Thyroids.**—The picture sketched above may be modified by the following secondary changes, especially in the nodular colloid types.

(*a*) Connective tissue hyperplasia. Goitrous nodules may be surrounded by firm fibrous capsules. The interstitial tissue of diffuse colloid goiters may become hyperplastic, as observed after injection of iodine. It is then a fibrous goiter of very firm consistency.

(*b*) Cyst formation. It has been mentioned that the disappearance of dividing walls in colloid goiters causes the formation of cysts, especially of the nodular type. Their contents may be watery, or colloid with later softening; fatty degeneration, calcification, hemorrhages due to disintegration of dividing walls, all combine to change the color to yellow, brown or red. Inflammation of the cyst walls causes their contents to become purulent; atrophy of the cysts may follow by granulation tissue and cicatrization.

In goiters with much colloid, fatty degeneration or softening may cause the cysts (liquefaction cysts). Interacinar and interstitial hemorrhages develop pictures in which the acini almost float in the liquefied interstitial tissue, to perish there. The cysts are often as large as a fist, and filled with a brownish smeary substance containing much cholesterin. In the older ones, the walls are thickened and surrounded by stratified connective tissue lamellae, probably calcified and uneven within, resembling an old aneurysmal sac. Occasionally, a papilliferous growth springs

from the inner cyst wall—papilliferous cyst adenoma—with the excrescences covered by cylindrical epithelium; larger cysts are usually lined with flat epithelium although some do not show this characteristic. Subepithelial psammoma granules can be found within (lit. Payr and Martina).

(*c*) If hemorrhages occur into the distended acini of a colloid cystic goiter, the contents become stained, as previously mentioned, or decompose into a brownish, smeary, necrotic mass, rich in cholesterin. Not rarely, there are pigment granule cells and giant cell collections around cholesterin plates. Fibrin and red blood corpuscles form firm, elastic, hyalin masses—the so-called rubber hyalin (v. Sinner, lit.). Hemorrhages into the interstitial tissue also cause cysts. Numerous larger hemorrhages lead to rapid formation of cystic hemorrhagic goiters.

Fig. 227.—Skeleton of a nodular goiter, chiefly capsular ossification. Nat. size.

Arteriosclerosis of the thyroid arteries is frequent, isolated, or as a part of a general arteriosclerosis (Abe).

(*d*) Calcification is very frequent, especially in fibrous and hyalinized interstitial tissue, less frequent in the changed acinar contents. Psammoma granules are also seen. The distribution of the process may be such that the whole goiter becomes stony hard, or stony nodules develop, or coral-like structures, or shell-like calcification of the capsule (calculus goiter). Goiters with inflammation present are especially prone to undergo calcification on account of the necrosis of tissue parts. True ossification (osseous goiter) is also quite frequent, (investigations of Sehrt, Hunziker and Pfister). Fig. 227 shows the skeleton of an ossified nodule.

(*e*) Hyalin degeneration of the interstitial tissue is often found. By van Gieson's method, it stains red, while the colloid is yellow to brown. In adenomatous nodules, the central portion is favored, as is the case in

all degenerative changes (Kraemer, Simpson). Amyloid is deposited in general amyloidosis chiefly in the vessels of the goiter (amyloid goiter). Rarely, amyloid is responsible for a goiter, *i.e.*, enlargement; it may be deposited without previous hypertrophy (v. Eiselsberg, lit.). The author saw amyloid infiltration everywhere in the vascular connective tissue apparatus of the thyroid. (Details and lit. in respect to thyroid amyloid by Schilder, see also Stoffel, Ipland.)

(*f*) See p. 509 for inflammation in goiters.

The effects of a goiter depend on its form and situation.

The most frequent and most dangerous result is compression of the trachea. Even small goiters cause compression symptoms if they grow a nularly around the trachea. Substernal goiters are especially dangerous, while the immense cystic goiters are least so, because of their tendency to hang downward in front. In unilateral goiter the trachea is laterally compressed or forced aside; in bilateral, the trachea, flattened on both sides, is shaped like the sheath of a knife.

According to Rose, pressure on the tracheal cartilages causes slow atrophy by general connective tissue replacement and fatty degeneration. He considered the sudden death from asphyxia in goiter operations due to occlusion of the flabby trachea minus its cartilaginous support. A lateral turn completely kinks it. Others, without good reason, think that this softening, found clinically by Denk and Hofer, occurs only in malignant goiters. But it is erroneous to believe that it is of special importance in "goiter-death," which is only an exception; kinking alone, without absorption of cartilage, can obstruct the lumen (cf. Henschen, lit.). The trachea is frequently distended below the stenosis (expiratory pressure).

The large vessels may become involved from pressure on the jugular veins, usually the external, or on the carotids; venous stasis and possible thrombosis occur in one case, and cerebral anemia in the other. Dislocation of the jugulars and carotids is frequent in larger goiters; the jugulars are pulled inward, the carotids pushed outward.

Pressure on nerves such as the vagus, sympathetic, and especially the recurrent laryngeal with paralysis of the laryngeal musculature, is also observed. Attacks of asphyxia are rare, hoarseness frequent (see de Quervain). The thin recurrent nerve which follows a side branch of the thyroid artery is endangered during operations, especially when the inferior thyroid artery is ligated during extirpation.

The esophagus is rarely involved to a noteworthy degree; at least, severe functional disturbances are infrequent (see p. 510 for exceptions, parastruma).

The muscles of the neck, the sterno-hyoids, sternothyroids and omohyoids, may be thinned by fatty degeneration from pressure.

By goiter heart (see Schanz and esp. Kraus, Chvostek, Bauer and lit. p. 77) is not meant the "dyspneic" hypertrophic heart caused mechanically by tracheal narrowing, bronchiectasis, and emphysema, and chiefly affecting the right ventricle; nor does it apply to the obstructive goiter heart caused by pressure on the veins and consequent congestion; we understand the true goiter heart to be thyrotoxic, affected from a distance by deviation of thyroid function, with frequent cooperation of the nerves which regulate heart action. This is the Basedow heart, and that produced by artificial hyperthyreosis. See Fahr in relation to changes in the heart muscle—(smaller and larger, mostly lymphocytic foci).

**Etiology. Cretinism, Cachexia Strumipriva. Myxedema.**—Goiter may be congenital. Glands belonging to this class have been seen by the author in Basel weighing up to 36 gms. Hesselberg also, who separates them into parenchymatous hyperplastic, and into teleangiectatic forms, mentions goiters that heavy. The normal weight according to the tables of Vierordt, is 4.85 gms.; according to our experience (Gottingen), it varies between 1 and 5 gms.; according to Hesselberg in Kiel, it is 1.55 gms., while in Bern, it is 6.6 gms. Goiter may also be acquired; it is more frequent in females and usually appears in youth. The congenital type may lead to sudden death from tracheal compression (see p. 498), assisted by venous stasis in the gland during the prone position (Kamann). The author saw familial occurrence (see also Schmidt); these are either parenchymatous or vascular (see also Krasnogorski, Staemmler). In contradistinction to Fabre and Thevenot, Hesselberg found the vascular type more frequent. On p. 509, we spoke of the influence of active and passive hyperemia on goiter formation; these are usually slight and the swellings only transitory.

Goiter occurs in endemic form in Switzerland, Tyrol, Styria, Carynthia, and in many other places; in such regions it may assume almost epidemic proportions. According to Isenschmidt (lit.), the thyroids of children in Bern are twice as heavy as those of the north German low plateau (see also Kloeppel, Sanderson-Damber); their acini are smaller, the nuclei larger and richer in chromatin. Goiter also appears sporadically. In reference to the etiology of endemic goiter, not one of the many suppositious infective factors have been found (see Kolle). Many think that there are local geological conditions, marine deposits of paleozoic age, at work, (lit. by Eug. Bircher; see also Ewald, Lobenhoffer, Pagenstecher), while according to Blauel, and the investigations of Dieterle, Hirschfeld and Klinger (lit.), the occurrence is independent of soil and water conditions, but locality, intercourse, and frequently also house and family conditions are of importance. This latter factor is especially emphasized by Kutschera who assumes there is contagion in a common

dwelling, and actually thinks of it as similar to Chaga's disease which is a goiter of inflammatory type (Viama and Wegelin; see p. 212). The infection is said to be carried by an intermediate host. Others, (Hirschfeld and Klinger, Landsteiner, Schlagenhaufer and v. Wagner), have failed to find contact infection of goiter to normal animals in a goiter-free locality. Not only are natives affected but also strangers, usually children, from healthy localities, who may, at times, after returning home, lose their beginning goiters (comp. Virchow, McCarrison and others). Domestic animals, dogs, sheep, calves and pigs, etc., become goitrous (lit. by Woudenberg). The drinking water has been held responsible, (Klebs and others); and it possibly has some influence, but thus far no real evidence is forthcoming. According to Klebs and H. Bircher, regulating the water supply successfully improved some cretinous, *i.e.*, goiter regions, a finding which has again been demonstrated by later investigations with endemic goiter. With so-called goiter-water, *i.e.*, water from goiter areas, Hirschfeld and Klinger and Eug. Bircher and Wilms produced thyroid enlargement in white rats, as a rule, diffuse parenchymatous goiters, rarely adenomas. The author himself verified this statement on Bircher's rat thyroids. They are quite similar to human forms (see Langhans and Wegelin, lit.). Heating is said to destroy the effect of the water, but this statement is contradicted by other observers. Wilms supposes its action is due to a toxin derived from organic deposits, but Grassi and Munaron came to a different conclusion on the basis of their successful experiments. They believe it is due to toxin producing "vital injurious substances" in the ground. On the other hand, Schlagenhaufer and Wagner v. Jauregg obtained no results with goiter waters in dogs (see appendix for Davidsohn, and lit. on experimental production of goiter). From the experiments with rats, variable though the results were, it can be seen that the development of goiter is not due to a single factor, *e.g.*, drinking water; indeed, local conditions and environment may be of greater importance. Rats kept in goitrous regions became goitrous, although they received no local water, while iodine administration prevented the goiter; on the other hand, in goiter-free areas, the drinking of goiter water gave no results. Rats react varyingly to injurious substances such as fecal matter supplied in their drinking water (Sasaki, McCarrison); in unpublished experiments, which the author conducted through Bauer, rats given infusions of manured earth reacted in the same way. In this case, it is possible to think of functional hyperplasia consequent to increased detoxifying activity of the thyroid. Nothing positive can be said, therefore, as to the cause of endemic goiter; the goiter problem remains unsolved. It may be the combination of an hereditary predisposition (see Behrens), with the immediate cause, a toxin, for instance

from a goitrous mother? (see Tausig). It is possible that this is transmitted in intrauterine life, but it is also possible that the increased predisposition is truly hereditary(?). A similar controversy rages about the character of the relationship beween the pathological thyroid and endemic cretinism (cf. criticism of Dieterle and lit. to chapt. 3 in appendix). Where ever there is cretinism, there is also goiter. Cretins are often, although not necessarily, found in the center of crowded goiter regions and since cretins are goitrous, we may assume that their thyroid secretion does not benefit them. On the other hand, the cretin may possess functioning thyroid tissue which may supply an abnormal secretion (W. Scholz, lit. and esp. Eug. Bircher, but see Getzowa also). The author can show this as a possibility by drawing on his own investigations; moreover, this view is supported by the fact that H. Bircher saw myxedema develop in two cretins whose goiters were removed. But others assume that the function of these thyroid glands is lowered, *i.e.*, there is "hypothyreosis." Wegelin (lit.), in typical adult cretins, found without exception, the thyroid gravely degenerated, sclerosed and atrophied, while on the other hand, in the goiters of non-cretins v. Werdt found the same lesions which were described by Coulon and Getzowa as occurring in cretins and idiots. Wagner von Jauregg in Styria, Eysselt in Moravia, Oswald in Switzerland report partial successes from treatment with thyroid gland (see criticisms by W. Scholz, lit., and Eug. Bircher). Eug. Bircher saw only negative results from implantations, a fact which even Th. Kocher, a staunch supporter of the thyrogenous theory of cretinism, cannot deny (see also Oswald). H. Bircher, who considers cretinism an intoxication, seems to us the most plausible reasoner. It may be an infection parallel to that of goiter, but occurring in higher degree in endemic regions; still it has not been proved that water is essential in this intoxication. In these regions the cretin-toxin causes goiter, endemic deafness and true cretinism to varying degrees (cf. Eug. Bircher). Parents of cretins often have goiters. But cretinism is not congenital and appears in the first to the second year of life. Opposing reports by Schlagenhaufer and Wagner von Jaureggs and others succumb under criticism. The changes of cretinism go hand in hand with cerebral lesions which may be equal to complete idiocy, even to anatomic brain findings (W. Scholz and Zingerle). There is also inhibition of body growth, especially of the skeleton, delayed dentition and delayed sexual development. The epiphyses remain as such for an abnormal length of time, (see under bones), constituting lesser degrees of disproportional dwarfism. Often there is concomitant "deaf mutism" (see Alexander).

If the thyroid atrophies from simple or inflammatory causes to a degree insufficient for the functional requirements of the organism, there develops myxedema, a grave condition chiefly affecting females. It was first

described in detail in England (Ord). There appears a peculiar swelling of the skin and subcutaneous tissue of the eyelids and face which later extends to the neck and extremities. The skin is pasty, pale, cold, it never sweats, and its blood supply is diminished. The swelling is said to be due to increased content of mucin, (lit. by Schlagenhaufer and Wagner v. Jauregg). The hair is sparse and dry. Growth of the long bones is diminished from bone changes (see v. Stubenrauch). Coincident symptoms develop in the nervous system, beginning with weakness of intellect, apathy, stupidity, increasing to idiocy. The congenital myxedema recognized soon after birth and infantile myxedema developing in the first years of life in those born perfectly healthy, myxidiocy, have been related to absence of the thyroid—athyreosis, thyreo-aplasia. In a number of cases, this was proved at autopsy, both grossly and microscopically, as in a case of the author, the second observed in Switzerland and reported by Dieterle (lit.); there was congenital aplasia of the thyroid. These congenital cases have been most unsuitably called sporadic cretinism; they display dwarfism, idiocy, myxedematous skin, thick lips and tongue, etc. This myxedema due to athyreosis, or, at least, to hypothyreosis, can be favorably influenced by thyroid preparations. Cures have been reported after thyroid implantation, after injection of thyroid gland juice, after ingesting thyroid substance in the form of tablets, and also after injection of thyreoiodin. See chapter on bones for skeletal changes in athyreosis.

Infantile mongolianism is often confused with myxedema and also cretinism. Mongolianism is characterized by numerous marks of degeneration, delayed dentition, small skull, small ears, etc., coupled with a congenital intellectual weakness. The physiognomic individuality becomes obliterated in the mongolian features. The cause of this developmental inhibition, which is no doubt general, is absolutely unknown. The author found the thyroid unchanged in this condition. Mongolianism differs from myxedema also by the absence of the characteristic skin and hair changes, by restlessness, sleeplessness, and failure of treatment with thyroid gland preparations (Kassowitz). The intellectual deficiency rarely reaches the degree of idiocy as found in athyreosis. Growth in length is not markedly influenced, (see Comby, Siegert, H. Vogt, lit., Weigandt, W. Scholz, Thomas, lit.).

After sudden and complete operative and experimental removal of the thyroid, severe nervous symptoms have been observed with tetany and spasms; involvement of respiratory musculature has caused a death resembling that of severe acute poisoning. Today we know that tetany results from the removal of the parathyroids, which was not always avoided during therapeutic or experimental thyroidectomy before the technique was perfected. Thyroidectomy brings about the chronic disturbances of

myxedema, but in both herbivorous and carnivorous animals, the removal of the parathyroids produces tetany, (Pineles, Gley, McCallum, Erdheim, Pfeiffer and Mayer; see also lit. by Schirmer and later experiments by Farner and Klinger). Careful investigations of athyreosis, children with complete thyroid aplasia, accompanied by myxedema, and who do not live beyond puberty (cf. Thomas, lit.), have demonstrated the presence of parathyroids in every case (lit. by Dieterle and Getzowa). The assumption of a vicarious activity of the parathyroids for the thyroid cannot be entertained (Gley, Kishi, see also Trautmann, lit.). In the most diverse species of animals, monkeys, rabbits, ruminants, carnivora, thyroidectomy produces severe chronic symptoms, leading eventually to death (lit. by Zietzschmann), but a small portion of functioning parenchyma can prevent these grave consequences. Bircher succeeded in apparently curing cases by thyroid implantation, but no increase of follicles in the transplant took place (Lubcke), or by the subcutaneous injection of thyroid gland juice, or by feeding thyroid gland. After some months or even years, however, there develop trophic disturbances of the skin, paleness, edema and inhibition of growth of the bones. Hofmeister removed the thyroid and parathyroids in young animals and obtained marked inhibition of growth in length, and marked delay in the ossification of epiphyseal cartilages and synchondroses (cf. chondro-dystrophia foetalis in chapter on bones; also details in reference to the skeleton of cretins). Then occur disturbances of general nutrition, weariness, loss of appetite, anemia, and foremost of all, disturbances of intelligence increasing to complete idiocy. Death occurs from progressive marasmus, usually in 4 to 5 years. Implantations into the spleen (Payr), into the metaphyses of the tibia (Th. Kocher, see also Sermann), or into the subcutaneous connective tissue (Carraro), do not guarantee extension of life and functional capacity of the transplanted thyroid (see also v. Eiselsberg, Payr; lit. by Paschoud). The post operative condition first described by Reverdin as myxedema operatoire, and by Th. Kocher as cachexia strumipriva, disease of the goiterless, or still better, cachexia thyreopriva, disease of those without thyroids, since the loss of the normal thyroid brings about the same consequences, is exactly similar to myxedema. But these thyreogenous diseases must not be identified with cretinism, even apart from the fact that in cretinism no thyroid disease can be demonstrated. Since thyroid implantation does not influence cretinism (Eug. Bircher), and since myxedema appears (H. Bircher) after removal of the goiter in cretins, the presence of deaf mutism and the different forms of mental deficiency in cretins cannot be considered due to the functional absence of the thyroid gland (cf. also Scholz).

If all the many experimental facts (since Horsley) in relation to the physiological importance of the thyroid gland are summed up, especially

from the pathological view point, there is, in the first place, no doubt that it is essential for the organism. But its activity cannot be simply characterized, as formerly, as detoxifying, serving merely to take care of injurious substances in the organism (Blum, in opposition, Kraus), because in thyroidectomized animals no poisons were found. The thyroid is really an endocrine gland of far wider importance. On the one hand, it functions in protein and fat catabolism, and on the other, it influences body growth. Apart from the anti-assimilating and assimilating influences, its secretory activity is extended to special functions. The vagus and the sympathetic system are stimulated, and the effect of adrenalin is strengthened by it. The details of these processes are made more difficult of interpretation by the fact that the thyroid is only a link in the chain of organs producing internal secretions or hormones or specific chemical stimulants, which are marvelously balanced and correlated in their stimulatory and inhibitory properties.

According to Oswald, the active specific secretion of the thyroid is iodothyreoglobulin. The thyroid gland contains two protein bodies: (1) the one just mentioned, an iodine-containing globulin, free from phosphorus; and (2) a phosphorous-containing iodine-free protein, a nucleoprotein; (1) is firmly bound to the colloid. The first product obtained from the thyroid gland by Baumann, iodothyrin, is an artificial decomposition product of the true secretion, and did not act as a life saver in the thyroidectomized goats of Pick and Pineles (see also Tschikste). The properties of iodothyreoglobulin, on the other hand, were in this respect identical to those of thyroid gland tissue itself. According to Grobly, the proteins retain the colloid, and insufficient production of them causes increased absorption of the total secretion leading to hyperthyreosis; this would occur in Basedow's disease (phosphorus therapy).

### Relation of the Thyroid Gland to Other Endocrine Organs

After thyroidectomy, the hypophysis, thymus and the adrenals show their reaction by enlargement. It is thought that there is a mutual inhibitory relation between the thyroid and the hypophysis cerebri, because the latter is often several times its normal size after thyroidectomy in rabbits and goats (the inhibition is removed). But it is questionable whether there is a vicarious process at work (see Staemmler, lit., Trautmann, Rossle). Inhibitory reactions occur also between thyroid and pancreas, for after removal of the pancreas, increased thyroid function has been observed, and vice versa, *i.e.*, inhibition of pancreatic activity in hyperthyreosis. Thyroidectomy affects the sexual glands; there is decrease of spermatogenesis and atrophy; conversely, after castration, there is marked diminution of the thyroid. H. Curschmann indeed saw myxe-

dema develop in a woman after operative castration. It is thought that the cooperation between the thyroid and thymus is of mutual benefit (see p. 501, and Faltan, Biedl, lit., Tsuji).

After operative or experimental removal of the thyroid with its myxedema, degenerative changes, especially in the ganglion cells of the anterior horns of the spinal cord, have been found; (see lit. by Isenschmid); this explains perhaps the absence of regeneration in destroyed peripheral nerves, as observed by Walder.

Literature to chapter 3 in appendix. [For tonsillar endamebiasis and thyroid disturbances, see Evans, J. S., Middleton, W. S. and Smith, A. J., Am. J. Med. Sci., 151: 210, 1916.—*Translator.*]

**Infectious Granulation Tumors.**—Tuberculosis is occasionally found in the form of miliary nodules in general miliary tuberculosis. Larger caseous masses are rarer in chronic tuberculosis of the thyroid, observed occasionally as primary tuberculous goiter (Bruns).

Inter- and intrafollicular localization of tubercles was seen by Ruppanner (lit.) and confirmed by the author. Hedinger thinks that tuberculous processes of the thyroid show an especial tendency to spontaneous healing. Besides hematogenous tuberculosis, a rarer form occurs by continuity from tuberculous lymph nodes. Tomellini produced tuberculosis experimentally, as did Shimodaire, who demonstrated less susceptibility, or more resistance than in other organs (see also Torri, Reinhart). In the course of phthisis, inflammatory swellings have been observed (Costa, v. Brandenstein), and de Quervain and Kehl describe sclerosis of the thyroid in this condition. Tuberculous goiter may be accompanied by symptoms of Basedow's disease (Uemura). Tubercles must not be confused with grouping of foreign body giant cells around colloid droplets (Wilke). In phthisis, the author saw yellow dots resembling miliary tubercles, but they were groups of alveoli with fatty degeneration of their contents (fat granule cells). (Lit. by Gebele, Kehl, Dutoid, Schoenberg, Nather.) For combination of goiter and carcinoma with tuberculosis, see Staemmler, Reinhart, (lit.).

Gummata are very rare and have been seen in the newborn.

Diffuse fibrous atrophy has also been described.

(For other facts, see Mendel, lit. by Rosenhauer.) [Also see case report by Groedel, F. M. and Hubert, G., Schweiz. Med. Wch., 1925, No. 29.—*Translator.*]

**Malignant Tumors Malignant Goiter.**—The main primary types are carcinoma and sarcoma; combination of both, sarco-carcinoma, is very rare, but the author has seen undoubted cases (see also Albrecht and others). Teratomas are even more rare, as the cases of Zahn and Wolfler and others (see lit. in appendix). The museum in Basle has a preparation of a tera-

toma removed from a newborn boy; it is the size of a fist, lobulated and partly cystic.

In goiter regions, *e.g.*, Switzerland, malignancy is frequent; it is usually suspected when a goiter steadily and unexplainably grows larger and harder with beginning and increased discomfort (Kocher). It sometimes appears early in the twenties, but is more frequent in later years, and according to de Quervain, is more common in males than females.

As exceptions, malignant goiters have occurred in children and even in the newborn (Zahn, O. Ehrhardt, lit.).

FIG. 228.—Carcinoma of the thyroid in a woman 68 years old. One year previously, a hard nodule was removed the size of a walnut. This had been present for considerable time but had grown rapidly in the course of a month before it was removed. At the end of a year the patient returned with a mass as shown. Careful examination, clinical and roentgenological, showed no evidence of metastases in the chest, nor were any nodules palpable over her body. The tumor was hard as a rock, fixed, slightly tender but superficially so, because of the thinning, redness and inflammation of the skin, rather than any deep seated tenderness. Such a tumor is interesting material for speculation and deduction on the biology of these growths. As stated in the text, the translator agrees wholely and fully with Graham when he states that the only way of diagnosing carcinoma of the thyroid is by finding thyroid carcinoma cells within blood vessels. Adenomas of the thyroid and, non-tumorous goiters are prone to all sorts of secondary changes and to such wild lawless-appearing pictures that the ordinary histological criteria of malignancy, as, for instance, in the breast, cannot be adopted. In other words, the translator would raise some doubt as to whether this tumor should be called carcinoma just because it recurred in such a form after a previous operation. Biologically in a year and one quarter, if these cells were very malignant, there should be metastases. L. H.

These malignant growths are to be differentiated from benign goiter grossly by their infiltration into adjacent tissue and their loss of mobility by adherence to neighboring organs, trachea, esophagus, etc. The author has often seen this criterion fail, however, especially in sarcomas; moreover, carcinomas, as v. Eiselberg emphasizes, may remain so small at times that they are overlooked clinically, and recognized first by metastases. General cachexia is usually absent, and cachexia thyreopriva is rare.

Nodular and diffuse, hard and soft carcinomas are differentiated. The nodular forms are more frequent, and may reach the size of a fist, rarely that of a child's head, or more. The hard forms remain relatively small at times (see above); the soft medullary forms grow very quickly, sometimes to enormous size. The color of the section surface is predominantly white, but becomes yellowish white, through fatty degeneration, and according to the vascular supply, necrosis and hemorrhage, gray-red to brown red.

FIG. 229.—Proliferating goiter (Langhans) (medium magn.).

Histologically, they are solid carcinoma simplex, or, more often, soft carcinomas; scrirrhous is very rare; adenocarcinomas show cylindrical or cuboid cells and may produce colloid. Adenocarcinomas, especially with epithelium resembling that of the thyroid, are sometimes difficult to distinguish from benign goiter if transition changes to carcinoma simplex or carcinoma cylindrocellulare are absent. The bone metastases may also appear like benign goiters, and such cases have been called "benign metastatic goiter," a designation which is, of course, not advisable (v. Eiselsberg).

Papillary adenocarcinomas are also encountered, though rarely. Squamous cell carcinoma is uncommon; it develops mostly in older goitrous individuals, rarely in children (Schmittmann, lit.), and arises from epithelium displaced from the primitive branchial cleft remains, or from the thyroglossal duct, or, not rarely, from pavement epithelium observed in the follicles and the interstitial tissue.

We are indebted to Langhans for his valuable investigations in reference to the forms of malignant epithelial goiter. He distinguishes (1) prolifer-

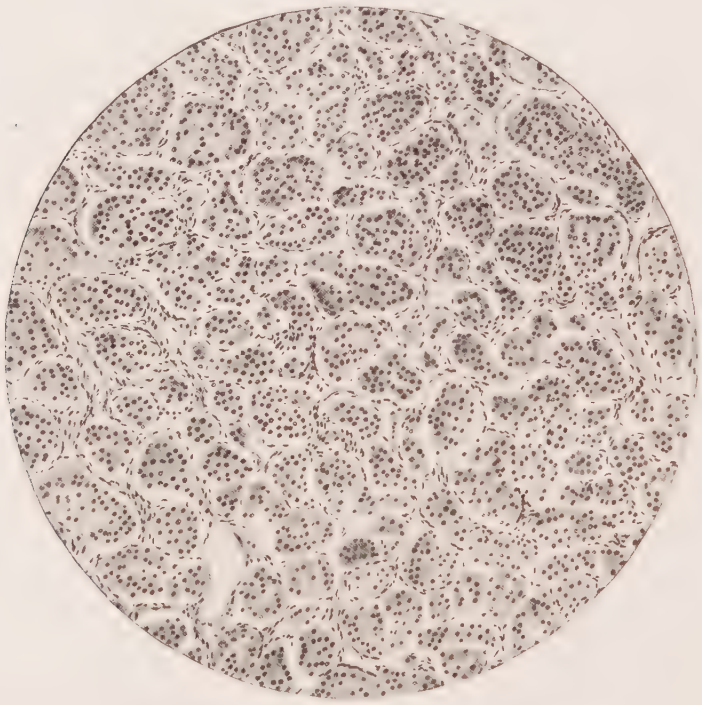


FIG. 230.—Postbranchial goiter (small alveolar, large cell goiter, Langhans) (medium magn.).

ating goiter; macroscopically, large encapsulated nodules do not perforate the goiter capsule and may reach a diameter of 15 cm. and more. The peripheral parts are lobulated with connective tissue septa. The centers show scars replacing destroyed tumor parenchyma, loose, resembling connective tissue and stellate in shape. The tumor tissue is soft, bulges outward, is moist, grayish red or pale (Langhans). The author has seen cases corresponding perfectly to this description. Microscopically, the solid masses of tightly packed epithelial cells in the periphery are divided by septa into separate groups and strands. Towards the center of these cell masses closely approximated spaces are formed; Langhans calls them "trellised fields," the author calls them "perforated masses;" they sepa-

rate, and when colloid accumulates, resemble normal thyroid gland. The peculiarity of this tumor, which, as Langhans emphasizes, is best understood in relation to normal development, justifies a special name; with its numerous acini and its malignancy, it might be called adenocarcinoma (Kocher). But Langhans never saw the lymph nodes invaded and metastases occur via blood stream. (2) Carcinomatous goiter shows the common irregular architecture of carcinoma. It is more nodular than number 1, the capsule is involved early, net-like cell strands quickly invade the reticular stroma. Kocher emphasizes the difficulty of distinguishing between (1) and (2) since, among other things, solid strands and masses of cells occur also in 1, and in 2 there are often scattered gland-like structures with colloid. In the author's experience the difficulty is only occasional. Zehbe supports the views of Langhans. There are cases in which differentiation between carcinoma and sarcoma becomes very difficult, (carcinoma pseudo-sarcomatosum, Wissmer). (3) Metastasizing colloid goiter. In the primary tumor and in the metastases the picture is that of common colloid goiter, but Langhans says there occur areas with solid cell strands in the metastases. Although Kocher is of the opinion that in this tumor also, there are transitions to (1) and (2), and that these latter may imitate the picture of so-called benign metastasizing goiter, he nevertheless places struma colloides maligna into a separate group, emphasizing the fact that pure "colloid goiter metastases" are possible from tumors which, either in the primary growth or its metastases or both, do not show the character of known malignant changes. Ehrhardt, Crone designate such cases as adenocarcinomas (see also v. Eiselsberg, who criticizes the name "benign metastasis;" also de Crignis, Thomsen). (4) Para struma. Tumors of parathyroids or their fragments misplaced within the thyroid gland (see Getzowa, Michaud, lit., Zehbe, Jaeger, lit.). This is the glycogen-containing goiter (Kocher, Jr.). Kocher, Sr., wants these called parastruma carcinomatosa or carcinoma parathyreoideum. They are lobulated alveolar structures with smaller cells containing fine glycogen droplets, or large water-clear cells with abundant glycogen, resembling the cells of hypernephromas, (Kocher, Jr.), but containing no fat. The appearance is that of acini also lined with high, water-clear, cylindric cells with nuclei situated at the free poles. The alveoli may be filled with abundant colloid. The combination with sarcoma has been observed in the primary tumor as well as in the metastases. (5) Struma postbranchialis (Getzowa) or small alveolar large cell goiter. These large cells resemble liver cells, or the fat-free cells of the adrenals. They are arranged very loosely into rounded masses, less often into strands. The stroma is delicate. Sometimes spaces and colloid are present. Macroscopically they are well encapsulated nodules, not differ-

ing from other nodular goiters. Their starting point is the postbranchial body, the so-called lateral thyroid gland anlage (see p. 506) Felsenstein, lit.). (6) Malignant papilloma, or better, malignant cyst papilloma. They give the impression of solid or cystic papillary tumors. Hemorrhage into tissue or cyst spaces is frequent. Kocher calls this cylindric cell tumor "adeno-carcinoma cylindrocellulare papillare," and "cyst carcinoma cylindrocellulare." The epithelium which covers the papillae with one or several layers is polymorphous and often considerably larger than normal with nuclei arranged close to the poles. The metastases show the same papillary structure. On the basis of his case, Zehbe considers no. 6 related to no. 1. Zullig describes four cases in which the malignant character was demonstrated by tumor nests in the capsules and the broader septa, where the cells formed masses, arranged into cavities. Getzowa would assign their origin to the branchial canals of the 3rd and 4th clefts, or to those of the post branchial body (see p. 506), and he speaks of them as branchial papillomata. (7) For squamous cell carcinoma, the so-called cancroid, see Kocher.

Sarcomas appear more frequently as unilateral or median tumors rather than diffuse forms. At times they grow very quickly, and occasionally enlarge rapidly from hemorrhages into the tumor tissue and necrosis, especially in round cell sarcoma. Histologically sarcomas differ greatly; there are large and small, round and spindle cell tumors. In a 56 year old woman, the author saw a fasciculated sarcoma with giant cells. Polymorphocellular sarcomas, sometimes with many giant cells, are rare but the author saw them in men of 54 and 58 years of age (see also Rijssel). Different forms of hemangiosarcomas, among them the rare peri- and hemangio-endotheliomas, either of alveolar or of cavernous structure, also occur (Limacher, Frattin, Hedinger, see also B. Muller, Winnen). The author observed a case of the latter variety (see Usui). Hedinger found a very extensive involvement of the veins, less so of the arteries, in sarcomatous goiters with exfoliation of the adventitia by invasion of tumor cells and consequent slit-like narrowing of the lumen. The author could verify these findings in a case of malignant goiter (see also Marro, lit.). Round cell sarcomas are considered exceptionally malignant. In one case in a 19 year old man, the rapid growth gave the impression of a phlegmon of the neck and metastases to the liver were present very early (observation of the author). Other forms, usually of vascular type, are frequently no less malignant. Fibro-, chondro-, osteo- and osteo-chondrosarcomas are more unusual (Funkenstein, lit.). There are also carcinosarcomas, *i.e.*, carcinomas with sarcomatous proliferation of the connective tissue substance, and both components may appear together or separate in the metastases. The author has also observed this.

As the malignant goiter grows, the form of the thyroid gland is often completely destroyed and the tumor masses extend into adjacent tissue. They often invade the veins of the neck, or penetrate the trachea, somewhat less frequently, the larynx; they infiltrate the muscles, at times, the skin; arteries are also eroded; nerves, recurrent or vagus, may be compressed and invaded. The more slowly growing carcinomas especially cause compression symptoms involving the trachea but also the esophagus, and these symptoms usually appear earlier than in benign goiter. Carcinomas and sarcomas metastasize both by the lymphatics and lymph nodes, but primarily and more frequently by the blood route, because they

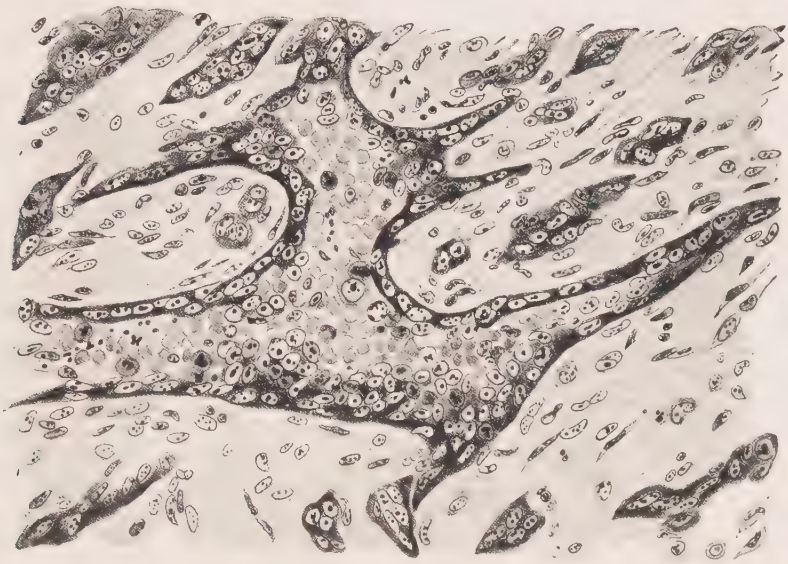


FIG. 231.—From metastasis to tibia of a sarcomatous hemagioendothelioma of the thyroid. The branching figure is a proliferating capillary blood-containing vessel showing in its lumen proliferating endothelium and outgrowths. In surrounding fibrous cortical tissue lie apparently isolated groups of very atypical sarcomatous endothelial cells. Consult for these tumors, p. 179. Man 62. Metastases to lungs, bones of extremities, roof of skull, lymph nodes. × 280.

invade the thyroid veins within the goiter and progress along their wall, or are released as emboli to the jugular; direct invasion of the jugular is less frequent. The hematogenous metastases involve the lungs and secondarily the skeletal system, without osteoplastic tendency, more rarely the liver, kidneys, stomach and bowel walls, etc.

The following observation from Basle illustrates the rapid growth and early metastasis in sarcomatous goiter. A sturdy 29 year old cooper weighing 77.73 kg. worked in his usual way up until 8 days before death, when respiratory difficulty appeared, and death occurred from edema of the glottis. At autopsy, a vascular polymorphocellular sarcoma with giant cells was found; it was the size of an egg; but in addition a number of

colloid goiter nodules as large as walnuts, contributed toward the enlargement of the thyroid. The trachea and thyroid vein were perforated by the growth, and in the right jugular vein was a tumor as large as an egg. Numerous tumor occlusions of the branches of the pulmonary artery and metastases in the lungs were also found, but no bone metastases. There was sarcomatous hemorrhagic pleuritis on the right side with 2.5 liters of almost pure blood in the pleural cavity.

The course is sometimes atypical, either (*a*) very rapid, more frequent with sarcoma than carcinoma (see above, observation of the author) or (*b*) very chronic, as sometimes in adenocarcinomas, or (*c*) the primary focus remains latent, while metastases dominate the picture.

The metastases to bones and other organs, rarely also in the skin (Fillie), may be multiple or solitary, and at times produce specific thyroid substances, (see p. 536 and M. B. Schmidt).

Carcinoma metastases often show great variation in their structure, compared to the primary tumor; they may have a more differentiated architecture similar to that of a benign colloid goiter, *i.e.*, metastases of so-called benign goiters, (Patel), but at other times the metastasis is more atypical, even to actual solid carcinoma. It is difficult to decide whether, as Gierke assumes, destructive "bone goiters" develop from gland cells carried away from a benign goiter, but it does not seem impossible. K. Ewald demonstrated the presence of iodothyrin in thyroid carcinomas and their metastases (see p. 528).

Metastases to the lungs may lead to erosion of vessels and perforation of the bronchi causing pulmonary hemorrhages and hemoptysis. In Basle, a 7th month pregnant factory worker, 28 years of age, developed adenocarcinoma with colloid formation, in an older nodular goiter. The pulmonary hemorrhages led to the wrong diagnosis of phthisis. The only metastases found were in the broncho-tracheal glands, and in two of the ribs.

According to the experience of the institute of Bern in reference to the frequency of bone metastases, the only other tumor which gives the same high percentage is mammary carcinoma (Limacher). According to the author's experience (Institute Basle), bone metastases in mammary carcinomas occurred in 52.3% of the cases, but prostatic carcinoma metastases, mostly osteoplastic in nature, exceeded this figure by 26.6%; in 29 thyroid carcinomas, 10 bone metastases were found—34.4% (cf. I. D. Nisnjewitsch, Basle, 1907). Pulsating bone metastases are unusual, but have been reported by O. Ehrhardt (lit.). The author saw this condition in a woman 63 years old; a carcinomatous goiter the size of a small apple perforated the superior thyroid vein; there were numerous nodules in the lungs, soft, moist, reddish, homogeneous metastases in the right

femur with fracture of its neck, in one rib, and in the spinous process of the 3rd lumbar vertebra. During life the bone metastases were palpable as pulsating tumors. Occasionally only one bone is the seat of metastasis, *e.g.*, the ileum (Paltauf, also the author), or the sternum, and the primary tumor in the thyroid gland may be overlooked. Kocher thinks that the chief areas of localization are the skull, manubrium sterni and ribs.

Secondary metastatic carcinomas and sarcomas of the thyroid are relatively rare, those from melanotic sarcomas more frequent, (experience of the author). Direct invasion of neighboring tumors, *e.g.*, from the trachea and the esophagus, has also been recorded.

From a primary ovarian carcinoma in a 59 year old woman, the author saw minute metastatic nodules only in a vascular adenoma of the thyroid and in no other part of the gland.

It is of interest to know that thyroid carcinoma occurs among the salmonidae, a group of fish to which salmon, trout, etc., belong, (L. Pick, Plehn, Schmey, lit., Plehn, and esp. Gaylord and Marsh). The injurious substance is said to be, not in the water, but in the bottom of the stream or lake.

**Translator's Remarks.**—As indicated in the text above, the diagnosis of carcinoma of the thyroid gland is quite difficult, grossly, because the hardness and fixation may be mimicked by calcification, hemorrhage, inflammation, etc., and microscopically because of the combination of hyperplasia and degenerative changes. According to Graham, with whom the translator agrees, the safest, and in fact almost the only single criterion beyond biological proof of metastasis, of malignancy of the thyroid is the discovery of invasion of blood vessels and tumor thrombosis; that is to say, all other microscopic pictures, no matter how atypical, may be of a biologically benign growth; but invasion into the blood vessels and appearance of tumor cells within their lumena means malignancy. Further, according to Graham, at least 90% of malignant epithelial tumors of the thyroid originate in preexisting adenomata. Such names as proliferating adenoma, metastasizing adenoma, metastasizing goiter, etc., are of course inappropriate; they are all carcinomas if they are biologically malignant and if they metastasize. See Graham, A., Surg., Gyn. and Obst., 39: 781, 1924 and Ann. of Surg., 81: 30, 1925.

Of *parasites*, only echinococci need be mentioned and they are quite rare. Their growth proceeds in exacerbations (v. Bergmann). Penetration into the trachea and larynx has been observed (lit. by v. Ultzmann, see also Landivar, A. Runge, lit.).

### Parathyroid Glands

The parathyroid glands or epithelial bodies have a local, but no special internal relation to the thyroid, as mentioned on p. 526 (see schematic fig. 219); they are independent endocrine organs (see also Biedl).

Generally, there are two on each side, a superior and an inferior, lying against the lateral lobes of the thyroid, posteriorly in close contact with the inferior thyroid artery at the place where the two terminal branches enter the thyroid. They are yellow to reddish brown, several millimeters long, but their size varies between 3 and 15 mm. Their number is also inconstant, sometimes there are 3, as many as 8 have been described; most of these accessory parathyroids belong to the lower glands. Although usually only loosely connected with the thyroid, they may, at least in part, lie within the capsule, or a single gland, an upper one, may be embedded within the organ (inner parathyroid). This is the rule in many animals. Histologically, they are composed of nests, follicle-like spaces and strands of epithelial cells surrounded by numerous wide capillaries and connective tissue. These small ductless endocrine glands are derived from epithelium of the 4th gill clefts. Some of the epithelial cells are flat in the cortical part, some are polygonal, others cylindrical, arranged follicular or gland-like. In the lumen, *i.e.*, in the intercellular "ducts" a colloid-like product or substance may be present. In the epithelium may be distinguished: (1) chief cells, rather small, with dark nuclei, staining reddish pink with eosin with finely granular protoplasm, or large water-clear, glycogen-containing cells; (2) cells with large granular or with homogeneous protoplasm staining intensively with eosin frequently lying in groups and oxyphilic in nature (Welsh); these are seldom present in younger children. Nothing certain can be said of their physiological importance; many interpret their presence as an expression of functional overactivity of the gland, (see Tomasqewski). Finally (3) there are syncytial cell groups composed of chief cells. Increasing with age, fat granules appear in the epithelium (details with lit. in the appendix).

Thymus lobules are frequently found in the neighborhood of the lower parathyroids, and a lower parathyroid, or parathyroid fragment may be included within the thymus gland. In rabbits, accessory parathyroids within the thymus gland may be so important that tetany develops after removal of the thymus (see Haberfeld and Schilder).

Getzowa and Michaud (see p. 533) reported isolated parathyroid cell masses in thyroids of cretins and idiots, also in non-atrophic thyroid glands.

Malignant tumors said to have arisen in the parathyroids have also been described (Benjamins, McCallum, Erdheim, Hulst, Verebely).

See p. 533, under carcinoma of the thyroid, in reference to paragoiters from intrathyroid gland inclusions.

For tumor metastases in parathyroids, see Thompson.

**Physiology, and Pathological Physiology.**—On p. 527, we spoke of tetania parathyreopriva which occurs after removal of the parathyroids in man and animals, either by extirpation or destruction; it is thought that the parathyroids neutralize poisons, tetany poison, formed during metabolism and acting chiefly on the nervous system. If all parathyroid tissue is removed, the animals perish. Relation to disease of the parathyroids has been suspected in the different forms of idiopathic tetany such as in maternity, menstruation, pregnancy, lactation, although sufficient anatomic investigations are lacking. In the tetanies based on gastro-intestinal and toxic disturbances, tuberculin, phosphorus and according to Fuchs, especially ergotin, the same may be said. On the other hand, we do not lack evidence in infantile tetany. Yanase and Haberfeld especially, have pointed to the frequency of hemorrhages caused by trauma or by asphyxia during birth, which cause tetany, not merely by tissue destruction, but more by the later disturbance in growth (hypoplasia) of the parathyroids and their functional deficiency. But others found the parathyroids intact in infantile tetany (Bliss, Thiemich, Jorgensen, Schiffer and others). Although Grosser and Betke negate the part played by hemorrhages in tetany, they hold them responsible for certain cases of sudden death in children. Auerbach found hemorrhages in 76% of all children, inclusive of those with tetany. McCallum therefore is not convinced that they bear any relation to tetany.

Implantation of parathyroids in animals after parathyroidectomy controlled the tetany, and was followed by cure; it therefore was used in the treatment of the tetany following goiter operations as well as in idiopathic tetany with some good results (see Leischner, Danielsen and D. u. Landois, Guleke, lit. Thierry, and in tetany of pregnancy, Phelps, Roth and others).

Numerous investigations deal with the relation of the parathyroids to calcium metabolism. In parathyroidectomized rats, Erdheim demonstrated disturbances in enamel formation, and particularly deficient dentin calcification of the gnawing teeth, causing them to break off. If a young rat had the parathyroids removed and immediately transplanted, (auto-transplantation), or if 12 days after a young rat had had its parathyroids destroyed by galvano cautery, those of another young rat were transplanted (homoio-transplantation) and then removed, the continuously growing gnawing teeth showed stripes deficient in lime, corresponding to the time in which the transplanted glands had not established themselves by healing, *i.e.*, while the animals had to live without them (see also Maggi, Hohlbaum, Toyofuku, Kranz). Erdheim, furthermore, showed that bone calcification is disturbed in young animals after extirpation of the para-

thyroids, and the newly formed tissue remains osteoid. Canal, Morel, Erdheim also found that after fracturing bones in parathyroidectomized rats, the callus contained very little lime. In cases of osteomalacia, hyperplasia of the parathyroids has been seen (Erdheim, Schmorl, Bauer, Strada, Todyo, Hohlbaum), and interpreted as an expression of increased function with increased calcium metabolism; this does not say the hyperplasia is the cause of osteomalacia, or of rickets, but the hyperplasia is secondary, the same as in the rickets of rats; it is a compensatory arrangement, or autotherapeutic effort against the basic disturbance, *i.e.*, the altered calcium metabolism. Erdheim and Tomaszewski (lit.) believe that this hyperplasia is the expression of the efforts of the organism to retain the equilibrium of calcium metabolism, to strive against demin-

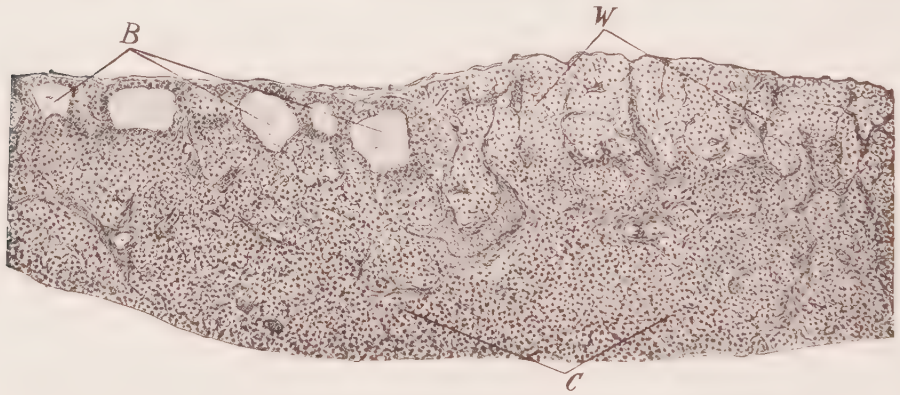



FIG. 232.—Parathyroids in tetany. Retardation of growth of a parathyroid gland by older blood cysts (B). W, area of growth with large light cells, absent at B. Child 5 months old, died of tetany. × 60. (Haberfeld, V.A. 203, 1911.)

eralization, and also to favor calcium deposit. But Bauer does not consider these explanations satisfactory, among other reasons, because hyperplasia is not constant in osteomalacia and rachitis. Hyperplasia has been found also in ostitis fibrosa, (Molineus, Maresch, Meyer and others), occasionally in senile osteoporosis, and even in individuals with healthy bone, (Todyo and others). In human rachitis, the findings were very inconstant, practically negative (for exceptions see Erdheim, Harbitz, Ritter). On the other hand, hyperplasia was found in spontaneous rachitis of rats (Erdheim, lit.); and dental changes also appeared, similar to those in parathyroidectomized rats. Fleischmann saw similar changes in the teeth of rachitic children, but considers them results of former tetany. MacCallum and Voegtlin demonstrated increased calcium excretion in urine and feces, and decreased calcium content of the blood in parathyroidectomized animals. Injection of calcium salts cured the tetany and hyperexcitability of the nerves. Improvement has occurred

in human tetany by this means. According to McCallum and Voegtlin, the increased calcium excretion is responsible for an acid intoxication with tetany as its consequence. Experimentally, Guleke discovered an antagonism between parathyroids and adrenals, and between parathyroids and thyroid, and believes the parathyroids by their antagonistic action hold the balance or counterbalance to these two organs which stimulate the sympathetic. If the adrenals were removed in animals whose parathyroids and thyroid have been extirpated, the tetany which resulted could be made to disappear. The lowering of the assimilation threshold for sugar demonstrated by R. Hirsch in tetany is comprehensible on account of adrenal predominance, consequent to the absence of parathyroid function; on the other hand, the success of calcium therapy would also be explained, since adrenalin destruction depends on the alkalinity of the blood. The tetany of pregnancy, from this point of view, might be explained perhaps by the frequently observed adrenal hypertrophy during pregnancy (see Guleke). See also experiments of Farner and Klinger.

**Translator's Remarks.**—Studies in which large numbers of rats were used indicate clearly that age and season are factors influencing the sensitivity of these animals to parathyroid deficiency (Hammett). There is good correlation between the reaction to these influences and the incidence of idiopathic tetany in man. These findings support the idea of a relationship between the disorder and inadequate parathyroid function.

Other factors influencing the resistance to the toxic effects of parathyroid deficiency as found by Hammett, are the weight, or state of nutrition of the animal at the time of parathyroid removal, and the relative excitability, or sensitivity of the instinctive reactions to external stimuli. The heavier or better nourished animals are more resistant, as are the less excitable. Later studies by Hammett indicate however, that in the albino rat at least, the lessened calcification is quite as much attributable to the retardation of growth of the bone as to a specific defect in calcium deposition. See:

Hammett, F. S. Studies of the thyroid apparatus. XLVIII. Age, sex, weight and season as lethal factors in conditions of parathyroid and thyroid deficiencies. Endocrinology, 1927, 11, 117–124.

Hammett, F. S. Studies of the thyroid apparatus. I. The stability of the nervous system as a factor in the resistance of the albino rat to the loss of the parathyroid secretion. Am. J. Physiol., 1921, 56, 196–204.

Hammett, F. S. Studies of the thyroid apparatus. XLV. The role of the thyroid and parathyroid glands in the chemical differentiation of bone during growth (calcium, magnesium, phosphorus). Studies of the thyroid apparatus. XLIV. The role of the thyroid and parathyroid glands in the chemical differentiation of bone during growth (ash, organic matter, and water). Journ. Biol. Chem., 1927, 72, 527–544; 505–525.

Furthermore that the parathyroid secretion has a definite influence on calcium has been proved by the use of the parathyroid preparation manufactured by Collip. See Collip and collaborators, International Clinics, Vol. 3, Series 35, 1925, p. 77 and J. Biol. Chem., 63: 395, 1925; 64: 485, 1925; 66: 133, 1925; 67: 679, 1926 and Am. J. of Physiology, 76: 472, 1926.

In paralysis agitans, Parkinson's disease, Roussy and Clunet found alterations in the parathyroids in the form of hyperplasia with much colloid and many acidophile cells to which they attribute a role of hyperfunction, particularly because in treatment with parathyroid, an exacerbation was noted (analogous to thyroid administration in Basedow's disease). But the same changes are also found in aged individuals and are not proof of hyperfunction (Biedl); others found no characteristic changes (see lit. by Bluwstein), and Koopmann (lit.) arrives at the conclusion that neither hyperfunction nor hypofunction of the parathyroids has been demonstrated in paralysis agitans.

In myasthenia gravis a correlation with disturbed parathyroid function is also considered, but Haberfeld denies this emphatically (for other points, see p. 503).

A relation of eclampsia to parathyroidea (insufficiency, Vassale) is probably not to be accepted (Seitz); (cf. also Biedl and lit. in appendix).

# CHAPTER IV

# DIGESTIVE ORGANS

## ORAL CAVITY

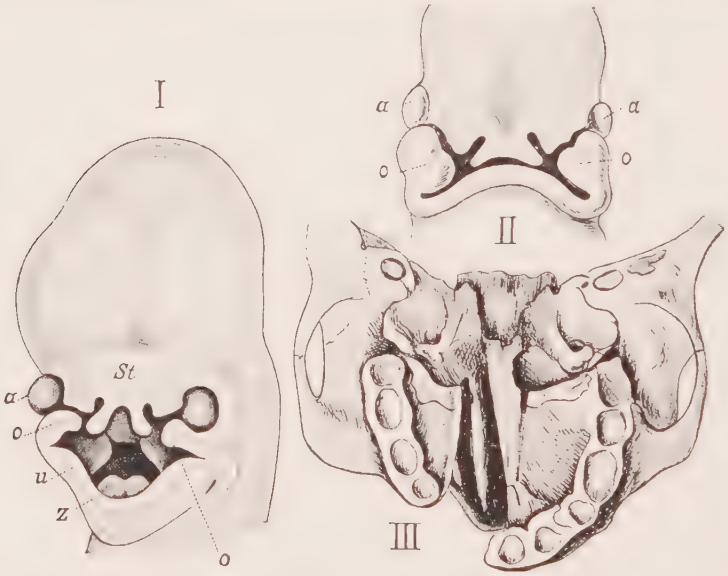
### MALFORMATIONS

Since the malformations of the mouth cavity are due most often to developmental interferences, it is necessary to rehearse some of the developmental history.

Toward the end of the third week there appear four openings on each of the lateral pharyngeal walls of the embryo, the gill clefts or gill furrows (p. 327); the protuberances bordering them are the gill arches. The last three gill clefts close during the first half of the second month thus completing the neck, *i.e.*, giving it its lateral walls, while the first pair becomes the auditory canal, tympanic cavity, and tube. The first gill arches (mandibular arch) unite in the median line with a prolongation growing downward from the frontal bone, and thus form the face. These prolongations have two processes on the median side, the superior and inferior maxillary processes; the latter grow toward each other and unite in the median line to form the inferior maxilla. The prolongations of the upper jaw do not meet in the median line, because the frontal process, with which they fuse, grows in between (fig. 233). This frontal process is laid down in four sections (figs. I and II), each two separated by the nasal fossa; the two median are longer and separated by an incisura (nasal fossa), but they soon fuse (dermoid, clefts, congenital scar formation in the center of the nose). Then they represent the constantly decreasing nasal septum between the nasal fossae, but they also supply the intermaxillary bone with the symmetrical intermaxillary lips (filtrum of upper lip). The two lateral, short and broad prolongations (external nasal processes) reach externally the oculo-nasal groove which closes to the nasal lacrymal duct; if this remains open, there is a congenital oblique facial cleft. The intermaxillary bone, the link connecting the superior maxillary processes, consists of two paired parts which soon fuse into two symmetrical bones; they carry the four (eventually six) incisors and for this reason are called incisor bones. While the intermaxillary bones remain separate in most animals, in man (as demonstrated by Goethe) they are intimately fused with the superior maxilla. The dorsal part of the first gill arch has two other flat prolongations—palatal plates, which

grow backward until they meet, forming the hard palate and uniting with the lower rim of the nasal septum and the intermaxillary bone (beginning of the third month). At the border of the intermaxillary bone and the palate, the incisor canal remains permanently. In this way the upper part of the primitive oral cavity is added to the nasal cavity as the respiratory part.

At the same time, the tongue develops on the floor of the oral cavity as a fold of mucosa, into which muscles grow. The lips develop as reduplications of the integument which covers the maxillae. These skin folds, becoming muscular, keep pace with the growth of the maxillary portions towards each other, until they unite in the median line as the lower lip, while in the upper lip the symmetrical filtrum grows downward with the




FIGS. 233 to 235.—I. Head of a human fetus 1.2 cm. long, magnified. a, eye; oo, superior maxillary processes; u, lower jaw; St. frontal process in the two broad, short lateral or outer, and the two lobed inner and middle nasal processes. Laterally and downward from the lower jaw to the left the aural anlage. Z, tongue. According to Dursy (Atlas of embryology of the head, Tubingen, 1866). II. Facial development of rabbit of 14 days; after His. a, eye; o, superior maxillary process. Otherwise drawing as in I. III. Left gnatho-palatoschisis (wolf's jaw). The nasal cavity with small portion of lower, and middle turbinate is seen through the defect in the alveolar process and hard palate. Vomer with intermaxillary bone is seen to the right of the cleft. After Bruns.

intermaxillary bone and pushes between the lateral parts of the upper lip. The posterior parts of these skin folds then fuse and form the cheeks. In this manner a new space is formed in front of the actual oral cavity, the horse shoe-shaped vestibule of the mouth.

Most malformations of the oral cavity are due to failure of union of parts which should grow to meet each other and fuse; thus they are clefts caused by primary malformations or embryonic disturbances due to amniotic adhesions (see fig. under amnion).

The most important are:

Labial clefts (cheilaschisis) or harelip; this most frequent cleft is caused by unilateral or bilateral failure of fusion of the filtrum of the upper lip descending between the intermaxillary bone and the lateral lip parts coming from the superior maxillary processes; the nasal furrow remains open on one or both sides. When bilateral, there are two clefts (fig. 236), one on each side of the median part of the upper lip; when unilateral, there is a right or left cleft. Exceptionally, the cleft is in the mid line due to the non closure of the median furrow between the nasal processes, or to defective structure of the filtrum. The cleft is more frequently on the left than the right; in fact, all clefts are more frequent on the left side. All degrees occur from a delicate crease (coloboma) to a complete fissure reaching into the nares. There are rare amniogenic harelips caused by amniotic bands (see fig. under amnion), but most labial clefts are due probably to a primary internal developmental fault in which heredity plays a recognizable part (Haymann, lit.).

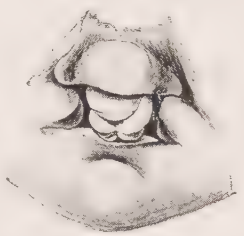


Fig. 236.—Bilateral hare lip, maxillary and palatal cleft (the latter not visible) in a child.

Other malformations may be present such as maxillary or palatine fissures, pedes valgi or vare, phimosis, etc., or even severer conditions, partly amniogenous, such as cerebral hernias (see fig. under amnion), snaring off of fingers, hexadactylism, duplication of the female genitalia, etc.

It is interesting to know that harelip may heal in utero with a faultless scar (Wolff). Facial clefts also may sometimes fuse in utero.

A cleft hard palate (gnathoschisis) and cleft soft palate sometimes accompany harelip.

The cleft in the hard palate is in the alveolar process of the superior maxilla between the outer incisor and canine teeth, corresponding to the fetal line of union between the process of the superior maxilla and the intermaxillary bone.

Cleft palate, palatochisis (fig. 235), may be present even though the external parts have united; the palatal plate of one or both sides fails to connect with the septum, and thus the cleft is lateral to this structure. When both the soft palate and uvula are cleft (frequent in gnatho-palatochisis), the fissure is median because both parts normally close in the mid line without the assistance of a bridge.

The exceptional median fissure in the hard palate is a defect, but not a cleft, because the parts which should have grown downward from the median nasal process, failed to develop at all. Consequently the filtrum of the upper lip is also absent, and there is a median defect of the lip.

If such cases are treated surgically, only one nostril, a median one, can be built.

Cheilo-gnatho-palatochisis (rictus lupinus) is a combination of the three fissures named (or only gnatho-palatochisis). When the cleft is unilateral the septum is usually connected to the side without the fissure, which also supports the intermaxillary bone. In bilateral fissure (fig. 236), the nasal septum protrudes free into the buccal cavity; the palatal plates may be only small ledges on the superior maxilla. The intermaxillary bone projects forward from the alveolar arch (prominent intermaxillary bone) or its growth is much inhibited.

The teeth (incisors) of the prominent intermaxillary bone are usually abnormal; often there are but two alveoli. The filtrum is a small prominence on the intermaxillary bone; the latter itself may appear like a proboscis.

**Other Facial Clefts.**—The oblique facial cleft (melochisis) involving the lip and cheek (p. 543) is very rare; the frontal process fails to unite on one or both sides with the intermaxillary bone; the fissure passes obliquely upward alongside the intermaxillary bone on one or both sides. The eye is situated at the posterior upper end of the deep cleft.

Transverse facial cleft, melochisis, macrostomia, congenital fissure of the mouth, horizontal cleft of the cheek, are designations for enlargement of the mouth which may continue to the ears.

Total facial cleft (prosopochisis schistoprosopy) is due to the frontal and supermaxillary processes remaining rudimentary. In the center of the face is a deep hollow which continues like wings to the eyes.

In median lip and palatal fissures, the intermaxillary bone remains very short, the two superior maxillary bones approach in the mid line without meeting.

Clefts of the median inferior maxilla and median lower lip are rare.

Among other disturbances of growth may be mentioned: microstomia, in which the union of the lips is too far toward the mid line and the mouth is too narrow (synchelia); microchelia, lips too short; ashelia, lips absent.

Agnathia, or absence of the lower jaw, may be due to faulty anlage of the symmetrical lower processes of the mandibular arch, or, according to v. Winckel, amniotic band (see amnion) compression or constriction of the lower jaw and its atrophy; at least, v. Winckel thus interpreted the findings of a rudiment of the jaw in cases of agnathia. But coincident malformations of internal organs suggest disturbances of the whole germinal anlage (Kuse). The mouth and the mouth cavity are small, the tongue is hypoplastic (microglossia), the pointed part is absent (Aschoff) and it lies back in the pharynx. The external and middle ears are close together,

nearer the mid line (synotia, otocephaly) and lie between the superior maxilla and the neck. In micrognathia (lit. by Trendelenburg), the upper and lower jaws are weakly developed (fig. 595), the tongue is normal and lies in the mouth cavity; in hemignathia, but half of the lower jaw is developed (lit. by Burger); both are rare.

Aprosopia, one of the severer developmental anomalies, is absence of the upper face; the frontal process and those of the superior maxilla remain rudimentary. The eyes at times are entirely undeveloped. The ears lie close together (synotia).

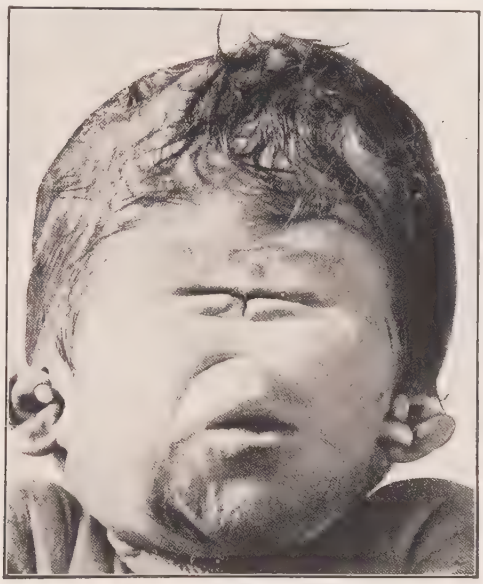


FIG. 237.—Cyclops. Synophthalmus with malformation of ears (accessory lobes).

In cyclopia there is a single eye with one optic nerve, or an apparently single eye which, in fact, is double (synophthalmia), *i.e.*, the eyes approach each other more or less and partially unite; the nose is absent, in its place is a skin fold, a proboscis-like structure, lying above the fused orbits; this is absent in fig. 237. The brain is always defective, the cerebral hemispheres may be represented by only a single cyst. The rhinencephalon (olfactory lobe) is absent (archinencephaly). Other malformations are usually present (lit. by E. v. Hippel, Josephy, Metman, Durlacher, Best).

For the structure and development of the mouth cavity, see G. Fischer; for the development of the face, see Peter, Keibel-Mall. Details and literature in ref. to malformations of the head by Grunberg, Schwalbe-Josephy, Josephy.

### Inflammations of the Buccal Cavity

A diffuse inflammation of the mouth (the mucosa) is called stomatitis; if only a part is affected, it is called accordingly, inflammation of the lips, cheilitis; gums, gingivitis; tongue, glossitis.

Inflammations of the teeth and their neighborhood, and of the salivary glands, will be discussed separately.

Erythema and Catarrhal Stomatitis, or Simplex. The first consists of redness which soon disappears, or becomes catarrhal stomatitis when the mucosa is both red and swollen, due primarily to irritants of a mechanical, thermal or chemical nature, or secondarily to ulcerative processes in the nose, pharynx, mouth, or acute infectious diseases (scarlet fever, measles, typhoid fever, etc.), or diseases of the stomach. A suppurative catarrh occurs in gonorrheal infections.

In desquamative catarrh, the mildest form of inflammation of the mucosa, there is much mucous secretion and epithelial desquamation; tags of connected pavement epithelium are detached from the lips, and exfoliation of the tongue causes the formation of a coating, white in simple cases, but often dirty brown and thick, *e.g.*, in typhoid fever. Food and medicine vary the color of the coating. The mucous glands enlarge, the lingual papillae swell, giving the surface of the tongue a granular or nodular appearance. Small cracks in the corners of the mouth and the middle of the lower lip bleed easily (chapped lips), become covered with crusts and may leave small ulcers.

In the characteristic tongue of scarlet-fever, the epithelium is exfoliated, first at the apex of the thickened and lengthened bright red papillae, later everywhere; the tongue is brilliant red, as though flayed; dry, shiny, with thickened papillae, separated by furrows (strawberry or raspberry tongue) (Hetzer).

Vesicular or pustular stomatitis is caused by the accumulation of exudate from vessels in or below the epithelial layers, wherever the mucosa is covered by a thick keratinized layer, such as on the lips, cheeks, tip of tongue. When such vesicles rupture, the erosion deepens to a small ulcer.

Etiologically, there should be considered: various irritants, caustics, burns, and progressive vesicular and pustular diseases of the skin, such as herpes, pemphigus, eczema, small-pox, erysipelas. It is worth remembering in the early diagnosis of small-pox, that the mucosa of the hard and soft palate is affected always and very early.

A vesicular stomatitis, accompanied by glossitis, resembling foot and mouth disease of cattle, may be transmitted to man (epidemic stomatitis). In children (adults frequently), even the milk of infected cows causes febrile digestive disturbances, and an expression of enterogenous general infection by vesicular stomatitis (cheilitis, glossitis); it is sometimes fatal

(Schossberger). The cause of the infection is unknown; Siegel's "cytorrhyctes aphthosis," a coccus, is probably no more responsible (C. Frankel) than the bodies seen enclosed in epithelium and in the vesicular lymph. Probably it is due to an ultramicroscopic, filtrable, transmissable virus (Loeffler). See the cases of Veiel (lit.). See A. Israel for local infection of the skin (foot disease in man).

Koplic spots, an important early symptom of measles, appear on the mucosa of the cheeks opposite the molar teeth some days before the eruption of the exanthem; they are minute, barely visible efflorescences to the size of pinheads, bluish-white in color, resembling whitewash spots with red edges (lit by Bruning). They disappear completely in 2 to 6 days. According to Hlava, they comprise a pustular exanthem, accompanied by cornification of the surface layers of epithelium (Ewing). They appear also on the lacrymal caruncles, according to Escherich, even before the spots in the mouth.

Pseudomembranous stomatitis is frequent at the root of the tongue in angina, especially scarlet fever angina.

A special form, aphthous stomatitis, occurs in the red mucosa of the mouth as cloudy white or yellow, rounded or oval, slightly raised spots, with blue red edges. The spots may appear in successive crops and heal quickly, most frequently in children during teething, but also in angina, pertussis, pneumonia, pregnant or puerperal anemic women; they are located on the tongue, lips, cheeks, and the transitions between gums and mucosa of cheek and tongue, while the gums themselves are but rarely involved. According to Eug. Fraenkel, it is a disseminated croupous inflammation in which a fibrinous exudate coagulates on the surface over the epithelium undergoing necrosis. It is doubtful whether the affection is of specific mycotic nature, for although various bacteria have been held responsible, the same organisms may be present in the healthy mouth cavity.

So-called Bednar's aphthae, appearing on the palate of small children, is differentiated from aphthous stomatitis, by the very regular symmetrical distribution of the oval, white yellow plaques or disks with red edges on both sides of the palatal vault. Their diameter rarely exceeds 1 cm. At first at the level of the mucosa, desquamation of the yellow gray base, especially in atrophic children, produces shallow ulcers which heal without scars, and rarely become deep.

They are considered due to mechanical factors (Henoch) such as trauma from suckling or wiping out the mouth. Some relate the typical localization to the so-called "milia" or epithelial pearls, cartilage-hard bodies, according to Peter, serving to fasten the fibrous base of the raphe; they are often seen in the newborn (95%, according to Fieux), and lying

alongside the raphe of the palatal vault, they may be compared to a barley corn slipped underneath the epithelium (Bednar). They are usually absorbed in time (months), but if the epithelial covering is lost, suppuration and ulceration take place. Most pediatrists consider the disintegration of the nodules due to unsuitable mouth hygiene. On the other hand, Eug. Fraenkel found the initial stage caused by bacterial removal of the upper epithelial layers (staphylococci or streptococci), *i.e.*, a primary mycotic epithelial necrosis followed by loss of epithelium and inflammation of the subepithelial layers, *i.e.*, ulceration.

Phlegmonous stomatitis, suppurative inflammations.

Phlegmon of the lips, phlegmonous cheilitis, may develop, among other conditions, after operative procedures and tumors. It begins with serous exudation into the tissues, increasing to suppuration; the lip becomes firm, tense, shiny, reddened. The so-called scrofulous hypertrophy of the lips is a chronic phlegmon, especially of the upper lip; the thickened hard tissue is covered with eczema, small ulcers and crusts. Microscopically, the lymphatics and connective tissue meshes are filled with fluid, the connective tissue is thickened and shows small cell infiltration (p. 260).

A phlegmon of the tongue (phlegmonous glossitis), glossitis profunda, may develop as a wound infection (cut, bite), or in erysipelas; the tongue becomes hard and thick and shows impressions of the teeth at its margins. The submucous tissue and the intermuscular septa are saturated with a cloudy, serosanguinous or purulent fluid. Later, a localized abscess may be felt as a hard, usually painless, nodule, rarely larger than a hazel nut. Sometimes the phlegmon heals by fibrous induration. Localized abscesses may also be caused by foreign bodies (fish bones, grain barbs).

Anerobic bacteria are active in gas-containing abscesses and extensive crackling phlegmons (Rodella, lit.).

Ulcerative stomatitis, stomacace, is an inflammation beginning with serosanguinous infiltration and ending in ulcerative disintegration, beginning in the gums and leading to extensive destruction of the mouth. It occurs occasionally as an epidemic in children's hospitals, especially during dentition, and is called idiopathic stomatitis; healing is the usual outcome. It is etiologically related to Plaut-Vincent's angina (p. 613) (comp. Buday)

In scurvy the inflammation is often hemorrhagic. The gums swell to. soft, blue red masses over the teeth, and may disintegrate to a brown green fetid poultaceous liquefaction which can be wiped away; after its removal the maxilla is exposed and the teeth may fall out, especially if the maxilla becomes necrotic. See Weigele for the various changes of the gums in scurvy; see Stepp in reference to scurvy as a whole.

In certain forms of poisoning, such as mercury, lead (saturnism), copper, phosphorus, the gums become red, swollen and cover the teeth; a gray to

brown black edge appears and the gums disintegrate into a fetid mass. Such ulcerative changes may progress to the mucosa of the cheeks. In severer cases the teeth fall out or the jaw undergoes necrosis. (More details of phosphorous necrosis under bones.)

Spindle-shaped (fusiform) gram-positive bacilli (details by Babes, Buday, lit.), in conjunction with gram-negative spirochetae of the type of mouth spirochetae (both protein-splitting), are found in abundance in various forms of membrano-ulcerative stomatitis with fetid disintegration; they are often present in pure culture, but may be found in less numbers as saprophytes even in a well-cared-for mouth cavity (Miller, Rona, Gerber). According to Gerber, these saprophytes become more numerous and pathogenic in general nutritional disturbances. Weinhardt considers the fusiform bacillus alone as pathogenic and invasive. More details under parasites of the mouth cavity (p. 560) and under Plaut-Vincent's angina (p. 613).

The deposit of the lead line consists of lead sulphide, and is most plentiful in the apices of the papillae, in the capillary endothelium and their immediate neighborhood. According to Fagge and H. Ruge, in chronic lead poisoning (saturnism) the metal probably circulating in the blood as a soluble albuminate of lead reaches the mucosa, is changed in the superficial parts of the gums by the sulphuretted hydrogen of the mouth into black lead sulphide and deposited as such. The chief portal of entry of the lead is the digestive tract (for analysis of feces, see Welwart). The typical localization is on the free edges of the gums, especially around the incisors, but also in the mucosa of the cheeks, rarely of the lips (Knierim, lit.). See Blum for industrial plumbism, and Schnitter, early recognition by examination of the blood (basophilic degeneration of erythrocytes).

Mercurial stomatitis occurs usually after the metal has been taken for some time. The changes vary from reddening, swelling, erosions, and ulcerations with purulent exudate, to gangrene (histology by Letulle) and necrosis of the jaw (Herzstein and Baer, Rocher). Individual susceptibility is an important factor in relation to the toxicity of mercury preparations however they may enter the body. In some people, a small amount of sublimate solution applied to a wound produces toxic symptoms (salivation, diarrhea, stomatitis); indeed, the author autopsied a case (published by Sackur) in which death occurred with all the symptoms of very severe mercury poisoning, after only one inunction with gray ointment, and that on the hand. Even inunctions for pediculosis pubis, etc., have produced fatal mercury poisoning (Wolfenstein, lit.). In others, even long continued use of mercury develops no stomatitis. Good mouth hygiene, especially of the teeth, is an essential precaution. Mercurial stomatitis is accompanied by excessive salivary secretion (ptyalism), and

some of the mercury which enters the body is excreted in the saliva. See Almkvist (lit.) and mercury poisoning under stomach, intestines, kidneys.

Noma, water cancer, cancer aquaticus.

According to Celsus, cancer is a gangrenous ulceration and was sharply differentiated by him from carcinoma. Later cancer became chancre, but the French and English used "cancer" to signify a malignant (epithelial) tumor, *i.e.*, carcinoma. The attempt to introduce "cancer" into German nomenclature is not advisable, since the term carcinoma answers all purposes.

Noma is a special form of ulcerative stomatitis, characterized by its tendency to extension, occurring almost exclusively in children (from 2 to 12 years old) and very rarely in adults (lit. by Weiss). It starts as cellulo-

FIGS. 238 and 239.—Noma. Casts at the pathol. inst. Gottingen.

edematous infiltration of the mucosa, usually near the angles of the mouth; as the tissues become gangrenous, the blue black, dry mass is cast off, but the disease progresses into the depths and laterally, quickly invading lips, skin and cheeks. Rapidly, in a few days, there is great loss of substance; the bones are exposed and undergo necrosis. Perforation of the cheek is especially characteristic and may occur in a few days, beginning as a blue red to black spot with a red demarkation edge on the pale puffy cheek, sometimes with a blister. After the crust is thrown off, a sharp edged hole pierces the cheek and exposes the mouth cavity to view.

On the whole, noma is rare, and occurs usually in poorly nourished children. It may be preceded by infectious diseases such as measles, scarlet fever, typhoid fever, influenza, etc., (Portmann), or arise entirely spontaneously. The disease is accompanied by high fever and delirium, and usually ends fatally in 2 to 3 weeks (from aspiration pneumonia).

The following observation may serve as an example: a cachectic 5 year old girl had suffered from measles, diphtheria, and finally pneumonia

within seven months, remaining miserable in the interims. Noma developed, perforated the cheek to the size of a silver dollar in 14 days, progressed rapidly and death occurred from bronchopneumonia.

The etiology does not appear to be uniform. Large numbers of microorganisms fill the diseased tissues, but the observed bacterial findings vary considerably. Schimmelbusch, and Babes each described a special bacillus. According to Perthes, it is a streptothix; v. Ranke and others endorse this, also Pawlowsky, but Buday thinks it is due to a symbiosis of spirillae and the fusiform bacillus, as in Plaut-Vincent's angina (gums, p. 613), which is therefore only qualitatively differentiated from the fatal noma by its milder course (see p. 550, idiopathic mouth gangrene). The finding of diphtheria bacilli by Freimuth and Petruschky and others is interesting and cures were reported from the use of diphtheria antitoxin (comp. genital noma under vagina and the author's finding of diphtheria bacilli). (Lit. by Bruning, and bacteriology by Hofmann and Kuster, Herman, Rona, Feldmann, Babes, Rosenberger.)

Gangrenous stomatitis in leucemia is mentioned on p. 559.

Chronic Stomatitis. Chronic inflammations of the oral mucosa are principally of productive character. The epithelium becomes thickened and cornified to a greater or less extent, the mucosa is infiltrated, the lymph nodules are enlarged, the papillae are swollen. The enlarged filiform papillae give the tongue a furry appearance.

Gray or blue white, flat, or raised spots, very irregular in shape, like maps or blotches of oil paint, situated on the mucosa of the cheeks, tongue, and inner side of the lips, are called oral leucoplakia (Schwimmer), milk spots, smoker's plaques, opaline plaques, psoriasis or lingual and buccal ichthyosis. (There is also a melanoplakia oris, among other conditions in Addison's disease—see under adrenals.)

These consist of thickened epithelium with superficial cornification, while the lower parts of the mucosa show cellular infiltration to the deeper layers, including many plasma cells (fig. 246).

The base of the epithelial layer is often indistinct on account of the small cell infiltration (plasma cells) and because the epithelium forms ridges between the cellular infiltrated papillae.

This condition is usually found in chronic irritation, chiefly in smokers, alcoholics, syphilitics; the latter, if they are smokers are especially subject to the disease (Kopp). In individuals who chew tobacco, Pichler found brown pigment spots. Landouzy thinks that leucoplakia of the cheeks and lips is due primarily to syphilis and that smoking is merely a predisposing cause. Erb found leucoplakia in 60% of syphilitic and 30% of healthy smokers. Lieven postulates a relation to gout. Mechanical lesions during mastication may remove the thickened epithelial layers or

cause small cracks (rhagades); small painful ulcers heal readily, but become covered by a blue translucent epithelial coating. Intercurrent attacks of glossitis are frequent, the papillae enlarge, the interpapillary spaces deepen, the tongue becomes horny, hard, rough and cracked. If the thickened epithelial layers are detached in foci by mechanical means, etc., the deeper cracks and ulcers may be mistaken for tuberculosis, secondary syphilis or carcinoma. But carcinoma may develop on the base of leucoplakia, according to Fournier, in even ⅓ of the cases; it may be primarily multiple, or grow in one ulcer, the margins of which become indurated. Suspicion is attached to an area which becomes rugose or papillomatous! The tumor may also appear in a fissure.

On the so-called geographical tongue (resembling a map) are red, sharply demarkated, but slightly infiltrated spots of various sizes, chiefly on the margins and apex; they may be so thickly strewn that only narrow, dirty white or pale yellow epithelial frames and edges remain. The tongue is red, as though injured, and may have numerous oblique parallel rhagades, especially on the anterior margin. The etiology is under dispute; heredity has been observed (Klausner, lit.). According to Moller, Caspary and others, digestive, nutritional disturbances (anemia), according to Bochm (lit.), tuberculosis, play a part. Czerny relates it to an exudative diathesis (pp. 260 and 261), in fact, as one of the important symptoms. Parrot correlates it with hereditary syphilis, and differentiation from syphilis is very difficult on purely anatomic grounds; antisyphilitic treatment is without result (Lang). On the other hand, the author saw a geographical tongue in a young non-syphilitic girl healed perfectly after thorough repair of the teeth, with the exception of an oblique indented fold on the surface of the tongue (plicated tongue). This change is known under many names, among others, circumscribed exfoliation of the tongue (Unna), benign plaques (Caspary), marginal exfoliating glossitis (Lemonnier).

Lichen ruber planus buccalis (compare analogous changes under skin) is a condition in which low, silvery white, hard nodules, single or grouped, appear on the buccal mucosa. According to Landouzy, the affection is due to syphilis.

### Infectious Granulation Tumors

**Tuberculosis of the Mouth Cavity.**—Tuberculosis may be primary in the lips and tongue, but more frequently secondary to infection by tubercle bacillus—containing sputa in ulcerative pulmonary tuberculosis.

Minute lesions of the mucosa, *e.g.*, from carious teeth or bites, may be inoculated with bacilli; the subsequent tubercles soon break down into shallow or deep ulcers (*a*) with flat, undermined, overhanging, sometimes

moth eaten margins. The edges not rarely are papilliferous, the epithelium blue white and thickened. The lateral edges and anterior part of the tongue are preferred. Occasionally tuberculous ulcers, often extensive, occur on the cheeks and elsewhere. In the tongue, the bacilli invade the lymph spaces between the muscle bundles, and deep in the musculature the tubercles are arranged like a string of beads.

Macroscopic tubercles can sometimes be seen in the bases of large tuberculous ulcers, like chains of beads and nets, while in smaller ulcers, the bases are often uniformly cheesy. If the nodules within the tongue are close and numerous the infiltrated areas are hardened (approximating form *b*). They are often mistaken for carcinoma (!) or lues, but the

FIG. 240.—Tuberculosis of the musculature of the tongue which is cut in various directions Two polynuclear giant cells, each in the centre of a cellular-fibrous tubercle; between them bundles of muscle cut across. To the right, tuberculous tissue with caseous center. Small cell infiltration in periphery of tubercles and between muscle bundles. From the vicinity of a tuberculous ulcer which had been taken clinically for carcinoma (medium magn.).

margins and bases of tuberculous ulcers are not usually as hard as those of carcinoma and the ulcers are often intensely painful. Swelling of lymph nodes may be present.

The deep form is rare, *i.e.*, a tuberculous nodule (*b*) in the depths of the tongue; from this may arise a sharply demarkated tuberculous (cold) abscess with fistulous rupture (mistaken for carcinoma or gumma). Primary tuberculosis of the gums is rare (v. Tappeiner, lit.). Literature on tuberculosis of the tongue by Scott. [See also Durante, L., Ann. Surg., 63: 143: 1916.—*Translator.*]

**Lupus,** the designation of an especially chronic form of tuberculosis which develops on the tongue and oral mucosa, especially the cheek, and is very poor in bacilli, appears in the form of pale ulcers with finely nodular, papillomatous margins, or as smooth nodules on hard bases, distinguished by marked scar tissue formation (pp. 297 and 316). Lupus may progress

to the pharynx and larynx. Carcinoma may develop in lupus (lupus carcinoma). Kren describes erythematous lupus which appears on the mucosa of the cheeks between the rows of teeth as dull red plaques with white dots and striae, the centers subject to erosion, the margins blue white, slightly raised, with red edges or gradually blending into white striations. The differential diagnosis should consider leucoplakia and syphilis. Therapy is powerless.

**Syphilis of the Oral Cavity** (see also p. 317).— Syphilis of the oral structures is frequent and takes various forms:

Primary lesions present themselves as scleroses or papules on the lips, angles of the mouth, tongue (apex) and sometimes even on the tonsils (p. 620).

Chancre of the lips is probably the most frequent extragenital primary lesion of syphilis (Bloch). Sometimes both lips are involved at once. Kissing is the chief mode of transmission, occasionally, feeding from mouth to mouth of luetic babies, through drinking glasses, cigar ends, pipes, blow pipes (glass blowers), etc. Indurative swelling of the submaxillary lymph nodes is present.

It has been repeatedly observed that areas occupied by a primary lesion later developed carcinoma, as, for instance, the point of the tongue. These carcinomas seem to be especially malignant.

Erythemas (secondary lesions) appear in the form of circumscribed or diffuse, red or blue edged, but slightly infiltrated spots, which undergo red or white coated erosion, and irregular, very sensitive fissure formation.

Papules or broad condylomas, mucous patches, secondary lesions, are described under skin. They begin as small, red, flat, elevations above which the epithelium is blue or yellow, cloudy and thickened. They heal smoothly after the epithelium is thrown off, but there remains an indurated red base with transparent, pale, yellow red granules which have a white appearance here and there, due to epithelial thickening. Besides this, crusts and superficial small ulcers may be produced by mechanical and chemical injuries; they heal to irregular contracted scars. Deep ulcers are rare. Some call syphilitic mucous papules "opaline plaques" (p. 553).

Gummata (see illustr. under muscles) make their appearance in tertiary syphilis, usually in the form of hard lumps, deep in the musculature, rarely in the submucosa. As a rule, tuberculosis is on the surface, at first, as small nodules. The palate, but particularly the tongue, especially the dorsal portion, are the sites of election, and they may be palpated as firm, elastic (painful), often multiple nodules, sometimes as large as a pigeon's egg. Gummas reaching the surface, break down into deep, funnel shaped, often irregularly pronged ulcers with undermined edges. Bacony, yellow white tissue comprises the bases. Since the disintegrating gummatous

proliferations often rupture on the surface of the tongue, the latter may appear perforated, with only small bridges of normal tissue remaining.

Gummas of the lips are either circumscribed (especially the upper lip) or diffuse, when they are accompanied by considerable thickening of the entire lip.

Disintegrating gummas often perforate the palate (see under nose, p. 298). When deep seated gummas heal by absorption (potass. iodide treatment), there remain contracting and deforming scars, their centers sometimes containing gummatous material (fig. 150, p. 317).

Superficial ulcers heal to smooth white scars (smooth tongue) containing small remnants of papillae and mucous islands (fig. 151), to knitted, raised, white, firm cicatrices; both forms may be present in the one case (fig. 150).

So-called smooth atrophy of the mucosa of the base of the tongue, characterized by smoothness and thinness, due chiefly to the disappearance of its follicular glands, but also to increase of connective tissue, is the product of an interstitial inflammation due to syphilis, according to Lewin and Heller (true atrophy), while real scars are caused by gummatous ulcerative processes. Opinions are divided as to whether it is pathognomonic or not, denied by E. Fraenkel, Goldschmidt, etc.; others state that smooth atrophy is exclusively (Symmers) or very frequently (Milne) due to syphilis (occasionally to tuberculosis, etc.). But in itself, without other signs of syphilis, this change is hardly sufficient to justify the diagnosis of "tertiary lues." According to Skladny, smooth atrophy is quite frequent in congenital lues.

For the differential diagnosis between lues, tuberculosis and carcinoma, see under the latter; for syphilis, and syphilis-like diseases of the oral cavity, see the atlas of Zinsser.

*Leprosy* appears in the tuberous form on the mucosa of the oral cavity, similar to that of the skin. See Rikli and Jeanselme for lepromas of the tongue.

**Actinomycosis of the Mouth Cavity.**—The ray fungus (p. 466) may reach the mucosa on foreign bodies which penetrate the soft gums, mucosa of the cheeks, tongue, etc., (straw, grains, especially barley), or may lodge in carious teeth; it may also enter the wall of the esophagus, stomach or intestine to spread from there, usually by continuity, to the adjacent or more distant surroundings; it rarely is distributed by the hematogenous route.

In one case, Partsch demonstrated the presence of fungus colonies in sections of a dental root, and Partsch and Jachn describe the progress of the fungus in the peridontium. Lord found actinomyces so frequently in carious teeth, that he considers them an important factor in caries (Euler),

but v. Baracz doubts that carious teeth are the portal of entry for dissemination; Zitz believes they are, likewise Kantorowicz.

It must be remembered, that the fusiform bacillus (p. 560), especially in mixed infections, may grow to macroscopically visible fungus-like colonies which might be mistaken for the ray fungus (pseudoactinomycosis); the clinical course, anatomical condition (fistulae, sulphur yellow granulations), etc., also may resemble actinomycosis. Melchior described such fusiform spirillar invasion of the neck. A Gram stain of the colonies (preparations made by crushing) reveals the difference,—bacilli in fusiform—spirillosis, threads in actinomycosis (Coronine and Priesel, lit.).

See p. 466 for other avenues of entrance of actinomycosis.

In cattle, the most frequent site of infection is in the mucosa of the mouth. Fungi entering on grains quickly reach the alveolar process, especially of the lower jaw, calling forth granulations containing viable

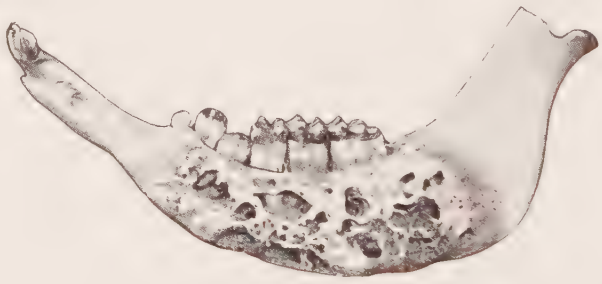


Fig. 241.—Actinomycosis of lower jaw of cow. The perforated tumor-like distension of the bone was filled with the specific granulations.

fungus colonies which tunnel into the bones in all directions; since new bone is laid down by the periosteum (a form of callus), considerable, spindle shaped expansion of the jaw takes place, with a striking resemblance to a myelogenous, shell sarcoma (fig. 241). In other cases, abscesses appear in the tongue and jaws. For the histology of actinomycosis of the tongue, lymph nodes, and jaws of cattle, see Joest and Zumpe, (lit.).

In man the primary, tumor-like, central, destructive and ossifying osteomyelitis of the jaw, so frequent in cattle, is quite rare (v. Baracz, Perthes, lit. Krymow, Zilz, lit.); the jaw is usually secondarily involved by a chronic periostitis with granulations and suppuration under the alveolar periosteum, and abscesses which rupture into the mouth cavity or perforate the outer skin. In the neck (cervico-buccal form) the infiltration of the subcutaneous tissues causes board-like hardness and the actinomycoma softens to blue to brown, characteristically stuffed looking elevations on firm bases. These rupture through many small fistulae or in one broad opening. The disease progressing downward as a board-like cicatricial infiltration perforated by fistulae and foci of softening, may

reach the spine and pleura or upward to the cranium and into it to the dura, soft membranes and the brain (see under bones). Actinomycosis of the superior maxilla may lock the jaws, involve the antrum of Highmore, extend to the base of the skull, or to the eye lids (rare). In clear cut cases, the lymph nodes are not involved (Partsch). The characteristic actinomycosis granules, usually sulphur-yellow, are found in the pus, or in the muco-gelatinous fluid of the granulations and fistulae (see p. 467).

Actinomycosis of the tongue may appear as a firm circumscribed nodule, or soft friable focus, usually at the apex, or as a diffuse firm, chronic abscess (mistaken for carcinoma—the actinomycotic abscess is softer and flatter—consider gumma). When the nodule softens, it leaves an ulcer in the vicinity of which new nodules and infiltrates are developed.

Actinomycosis of the lips is very rare (C. Koch, v. Baracz, lit.).

Individuals with actinomycosis, chiefly men, usually pursue agricultural and related occupations.

Lit. by Jachn, Shiota, Harbitz and Grondahl.

**Glanders.**—Glanders of the mouth cavity with ulcers, marked destruction, especially of the palate, is occasionally observed (Zieler). In the differential diagnosis, tuberculosis and syphilis must be considered.

**Appendix:** Leucemic Stomatitis.—This appears under variable pictures, sometimes like scurvy of the gums, especially in the acute lymphatic form (Marchand), or as pasty coatings of the tongue, or as gangrene of the mucosa, or as swelling of the mucosa, or as a tumor-like swelling of the adenoid tissue of the base of the tongue and the tonsils (Waldeyer's adenoid pharyngeal ring), as in fig. 277 (Askanazy). Infiltrations may become purulent and gangrenous and disintegrate to deep ulcers. According to the prevailing opinion, this takes place only in lymphatic leucemia (v. Domarus), but the author saw it in myeloblastic leucemia in a man 35 years old, in whom the purulent disintegration involved the left tonsil, the floor of the mouth, the edges of the tongue, inner side of lips, gums and the alveolar process of the lower jaw, which, with its loosened teeth resembled fig. 247. All the lymph nodules were moderately swollen, the bone marrow red; microscopic myeloid metamorphosis in lymph nodes (fig. 130, p. 263), spleen, bone marrow, and kidneys; oxydase reaction (p. 205) positive.

### Microorganisms of the Buccal Cavity

The quantity and variety of vegetable parasites which enter the mouth cavity with the air, food or otherwise, are very large; they include mould fungi, yeasts and fission fungi. Among the latter are found (even in the healthy) bacteria, which may become the causative factors of certain diseases in man. Thus, in the mouths of healthy people are found, at

times, the diplococcus and bacillus pneumoniae—Friedlander, bacillus pseudo-diphthericus (see under pharyngeal diphtheria), staphylococcus and streptococcus pyogenes, micrococcus tetragenus (lit. by van Rymsdyk), etc. Since they have potential pathogenic properties, as animal experiments show, it may be assumed that they occasionally leave the oral cavity for the respiratory and digestive tracts, and under suitable circumstances exhibit their pathogenic properties (comp. tetragenus and mixed infection in phthisis of the lungs).

Miller in his investigations of the mouth flora, mentions among the fungi present in the white coating of the teeth, a certain "leptothrix innominata," a nonarticulated thread-like microorganism; when scrapings from the teeth are examined in a solution of potassium iodide, slightly acidulated with lactic acid, this fungus stains yellow and is thus differentiated from other forms of leptothrix which are generally called leptothrix buccalis. Other fungi stain blue violet in this solution; the one form is called by Miller iodocoecus vaginatus (heaps or chains of cocci), the other, bacillus moximus buccalis (a thick bacillus). Among other fungi may be mentioned: spirillum sputigenum, the so-called comma bacillus, a curved organism, which, according to Muhlens, can be grown anaerobically in pure culture in horse-serum-agar; it is accompanied by the coarse spirocheta buccalis and the finer spirocheta dentium (lit. of spirochetae of the mouth and teeth by Hoffmann, staining by Becker); to these are added the bacillus fusiformis or lanceolate bacillus which is found abundantly in the coating of ulcers, specific or non specific; but all of these may be present in an absolutely normal pharyngeal cavity, and on the necks of the teeth, in the lacunae of the tonsils, and between the papillae of the tongue. Knowledge of the spirochetae of the oral cavity is quite important as a help in the difficult recognition of the spirocheta pallida of syphilis (Gerber). The last named bacteria are usually not pathogenic in the normal oral cavity; they are saprophytes which grow on exfoliated dead cells and food remains; they may, however, cause putrid decomposition, which in turn causes inflammation of the mucosa. Diseases like stomacace, noma, Plaut-Vincent's angina (p. 613) and necrotic lung processes, nevertheless show that they can become pathogenic. Tubercle bacilli are often present in the mouth, always in ulcerative tuberculosis of the lungs. This constitutes a source of infection (p. 456).

Among animal microorganisms the non-pathogenic entameba buccalis might be mentioned as a regular habitant of the mouth cavity (Kuster, W. Fischer).

Thrush mouth is due to the "oidium albicans" (also called mycoderma albicans); white or yellow, raised, easily removable spots appear chiefly on the tongue and the maxillary ridges after preceding redness; they may

coalesce to plaques several millimetres in thickness. The fungi rest on the mucosa, or more commonly, invade the epithelial layers and (parasitically) the epithelial cells. Old membranes become dirty gray, and are attached more firmly than recent growths; the non-covered parts of the mucosa are markedly reddened. If the epithelial cells in which these fungi proliferate should disintegrate in larger quantities, they leave small thrush ulcers.

The so-called thrush membrane consists of masses of doubly curved, glass-clear, articulated mycelium threads which often show glass-clear corpuscles in their protoplasm with short processes ending in clubbed, swollen ends intertwined with each other. In between are yeast-like, globular or cylindrical cells, conidia, from which oval or globular cells bud in rows; the latter often lie free and scattered (fig. 242). Between the fungi are always numerous exfoliated pavement epithelial cells, leucocytes and various bacteria, (fig. 242).

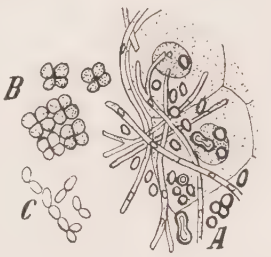



FIG. 242.—A, Oidium albicans of esophagus. Threads and conidia in epithelium and free. B, Sarcinae ventriculi; C, blastomycetes and saccharomyces for comparison.

Thrush occurs chiefly in nursing babies; sweet substances and fermentable material with abundant supply of oxygen favor growth of the organism. It is also frequently seen in ill-cared for, decrepit and feverish patients (phthisis, typhoid fever, etc.), and especially in diabetics. The oral mucosa may be exceedingly painful. Sometimes thrush is added to another disease, *e.g.*, diphtheria.

Other localizations are: the pharynx, esophagus, rarely the stomach, ileum, anus, nasal cavity, trachea, larynx, middle ear, vagina (also in small children) and the nipple of the nursing woman.

The fungi may reach the lung by aspiration and cause lobular pneumonia, not rare in nursing babies.

The threads of oidium albicans rarely enter the tissues of the mucosa, much less the blood vessels (E. Wagner), but they may be transported elsewhere and produce thrush pyemia. Zenker first described such metastatic implantation with multiple brain abscesses, among other things (Heubner). In a victim of typhoid fever, who also had diphtheritic crusts of the mouth, pharynx and esophagus, Schmorl observed that the fungus had been carried into the spleen and kidneys. Paltauf saw metastases in the brain and lungs from intestinal ulcers. Von Hibler described a thrush abscess of the brain. The thrush fungus is pathogenic for rabbits.

In the macroscopic differential diagnosis must be considered: remnants of milk which can be wiped away more easily than thrush (Henoch), diphtheritic membranes, which usually are much more firmly attached:

the differentiation becomes more difficult in older, pearl gray or yellow, firmly attached thrush membranes. The membrane-like coatings due to catarrhal exfoliation of the epithelium of the tongue or gums may also cause confusion.

The biological position of the thrush fungus is still disputed; according to Roux and Linossier, it is a mould fungus (mycelium) with a pronounced growth capacity in yeast conidia forms, but in a suitable pabulum producing mycelia (lit. by Plaut, clinical biology by Steinert).

## Tumor-like Hypertrophy and True Tumors of the Structures of the Oral Cavity

**Benign Structures in Soft Parts. Macrocheilia and Macroglossia.**—Macrocheilia, a congenital trouble, sometimes develops rapidly as a deforming enlargement of a lip, rarely, of one-half of a lip. The upper lip may resemble a proboscis or the lower lip may protrude like the spout of a jug. The change may be due (*a*) to hypertrophy of all parts; (*b*) to diffuse growth of connective tissue; the lip is hard, and grates on cutting; nodular connective tissue growth is rare; (*c*) to ectasia or new formation of lymph vessels—or both combined, between which more or less connective tissue is found containing small foci of lymphoid tissue (lymphangiectatic and lymphangiomatous macrocheilia). Sometimes the tongue participates in the enlargement (muzzle-like appearance of the mouth); also the lower jaw may be deformed.

In macroglossia the tongue enlarges partially or totally, and protrudes from the mouth (prolapsus linguae, glossocele); it may even become pendulous and reach the breast. The surface shows deep dental impressions. The tongue is permanently in front of the mouth, becomes dry, rough, and fissured, or covered with crusts, and bleeds easily. The teeth and alveolar processes may assume a horizontal direction, due to the pressure of the thick, forward-pressing tongue. It is usually a congenital trouble which quickly increases after birth, mostly in exacerbations. Congenital macroglossia may prevent respiration and alimentation in the new born. In most cases, the enlargement of the tongue is due to tumor-like growth of the lymphatics, *i.e.*, lymphangiomas (p. 177).

In many cases, the interstitial connective tissue and the muscle of the walls of the newly formed lymph vessels are markedly thickened, and the cellular interstitial tissue contains lymphoid foci. The blood vessels of the interstitial tissue may be especially well developed, or considerable collections of fat are found. The advent of inflammation from the surface, or by way of the lymphatics, causes acute, even dangerous, swelling (Kuttner).

Macroglossia may also be due to thin-walled cavernous blood vessels (cavernous hemangioma), or the walls between dilated lymph vessels and adjacent veins disappear from pressure, so that blood enters the lymph spaces in the mixed hemato-lymphangioma (Wegner, Meurmann). As in hemangiomas, the tongue becomes thick, dark, black blue, and on incision dark blood pours out in large quantities. Circumscribed lymphangiomas are rare.

For pure capillary teleangiectasis, see Meerwein.

Sometimes, macroglossia, partial or total, is due to hypertrophy of all parts, *e.g.*, in the newborn with "fetal chondrodystrophy," or in cretins (in conjunction with macrocheilia and prognathism). Otherwise, muscular macroglossia is rare (see Wetzel, lit.); in acromegaly, the tongue may be enlarged.

FIG. 243.—Cystic degeneration of fungiform lingual papillae; L, cystic dilatation of lymph vessels; E, epithelium of surface of tongue. Case mentioned in text (12 year old girl) (low power).

Neurofibromatous macroglossia, also congenital, has been described by Abbot, and Shattock, Delefosso, Delfino, Hayashi.

A rare and peculiar condition is cystic degeneration of the fungiform papillae of the tongue (Dollinger), a cystic or varicose dilatation of the lymph capillaries of these papillae. The surface of the tongue shows granules, vesicles and dots to the size of a poppy seed, blue white, sometimes pearly and cloudy, sometimes transparent, like dew drops, which correspond to the papillary apexes hollowed into thin walled, small cysts. The author saw a case in a 10 year old boy in whom the whole surface of the tongue, especially the marginal parts, was fissured, ragged and covered with granules and dots. The affection caused no discomfort. In another case, examined by the author (12 year old girl), the alleged two year old condition was confined to an area not much larger than a five cent piece. The papillae thickened and pear shaped were distended by lymph spaces. On the apex of the vesicles the surface epithelium was thin, but elsewhere quite considerably thickened (fig. 243).

The author saw the same microscopic picture in an 11 year old boy, also in a boy 5 years old whose tongue, in the center, slightly in front of the circumvallate papillae, showed a raised focus the size of a thumb nail. The collection of Basel possesses a similar specimen from a 14 year old girl. Such lymphatic varices (Tenneson and Darrier) also occur on the mucosa of the cheeks and lips. Robin and Leredde consider them due to repeated inflammation with occasional occlusion and congestive dilatation of lymph spaces. The author considers them more probably a congenital anomaly (Rehn); Sorentino speaks of cricumscribed lymphangioma of the tongue (papillo-cystic tongue; Schmerz).

So-called amyloid tumors (local tumor-like amyloid infiltration of the tongue, p. 323), sometimes multiple, are very rare (lit. by Gross, Heller, Schilder, Schonhof, Freckmann). The author examined a nummular amyloid tumor of the dorsum of the tongue in a 40 year old woman. The posterior segment is the favorite location. The differential diagnosis should consider carcinoma.

Plasmocytomas (p. 272) may be mistaken for true tumors. The author saw a plasmacellular granuloma the size of a pea on the lower lip of a 56 year old man.

**Benign Tumors of the Connective Tissue Group.**—Among these are fibromas of the mucosa, sometimes present for years, small, usually on the dorsal part of the tongue, rarely polypoid or pedunculated and on the point of tongue, occasionally multiple (Morestin), lipomas, fibrolipomas (point of tongue, lower lip on the mucosa side), myxomas, chondromas, osteomas; these are all rare, congenital, or develop in the first years of life. Angiomas, chiefly hemangiomas (spots, nodular tumors, fungiform or papillary), and lymphangiomas occasionally spring from any part of the oral cavity, especially from the lips (chiefly the upper lip), even in children. They may assume larger dimensions and penetrate underlying tissues, changing occasionally into sarcomas. Hemangiomas also occur in the tongue, especially in the tip, and may project like fungi; rarely they are erectile tumors of greater extent.

Fungoid, so-called telangiectic granulomas (granuloma pediculatium) (illustr. under skin), easily bleeding, must not be mistaken for true angiomas. The author has often seen them on the tongue and lips of older people, mostly women, and one on the lip of an 11 year old girl (Jessup, Luchs; opposed, Heise).

**Epithelial Hypertrophy and Tumors.**—In the so-called black hairy tongue, the filiform papillae lengthen from marked proliferation (hypertrophy) and cornification (hyperkeratosis) of their epithelium to bristly or thread-like structures looking like beds of moss. In a specimen at Basel, the brown-green threads had lengths of 1 cm. The black, brown to green

color is due to a diffuse discoloration of the cornified cells, purely chemical (from the moisture of the mouth, Oppenheim), and to ingested substances (Blogvad, Haenisch). Others consider the black hairy tongue due to proliferations of mold fungi (mucor) (Gueguen).

The author saw an unusual hyperkeratosis of the filiform (and fungiform) papillae in a 64 year old woman (contracted kidney, atheromatosis, no skin changes) which gave the surface of the broad tongue a peculiar appearance. The anterior part was white blue, rough, dry, and covered by dainty, short, beveled convolutions, 2 to 3 mm. broad, running chiefly across and symmetrically arranged with intervening furrows to 2 mm. in depth. The surface of these fairly equally high gyri was not convex, but flattened and thickly and evenly covered with the finest, hard, uniform granules; the sulci were clubbed or button-like larger granules. This affection gradually diminished posteriorly, and in the area of circumvallate papillae only dots and granules were seen as blue-white and soft spots. The edges of the tongue were furrowed and granular in the anterior part, and smooth in the posterior. There were no rhagades. Microscopically, there were marked thickening of the epithelial coating of the papillae and hyperkeratosis (but without kerato-hyalin). A second analogous observation concerned a 63 year old drinker, a third, a 28 year old man with a status lymphaticus. Mild cases are not rare. The scrotum-like condition of the tongue of Dubreuil-Chambardel seems to be similar, with some anatomical variations (Schmidt).

Papillary tumors, so-called papillomas (papillary epitheliomas or fibro-epitheliomas), are not rare on the tongue and lips. Hard warts covered with thick cornified epithelial layers on the epidermoid part of the lips are of practical importance, because they may be mistaken for carcinoma. Cutaneous horn growths appear occasionally on the lips, more rarely on the mucosa of the cheeks, perhaps in leucoplakia (Konjetzny), due to heaping up of abnormally cornified epithelium (epithelioma); these are composed, in circumscribed areas, of superimposed low papillae of varying breadth. Transition into carcinoma is possible, but its beginnings are hard to demonstrate clinically, although microscopically, it shows a solution into small plugs and invasion of the base.

Adenomas may spring from the mucous glands of lips, tongue and cheeks. Not rarely the neoplastic gland cells are accompanied by a colloid transformation of the epithelium. The so-called colloid tumor may be multiple; small transparent tumors can be shelled out. Small pedunculated adenomas may grow on the tongue; others are deep in the tissues.

Struma of the root of the tongue is rather rare; Walther was able to compile 70 cases; Asch speaks of 95. It may be called ectopic thyroid gland when the thyroid itself, in its normal place, is poorly, or not at all,

developed, or accessory thyroid when only a part of the thyroid anlage developed above, and the other part is in its normal place (cases of Galisch and others). The designation "aberrant struma" is an error. The cases were exclusively in young women, some of whom were myxedematous. The location of the growth, which may exceed the size of a walnut and is sharply circumscribed, corresponds to the area of the foramen cecum in front of the epiglottis. Histologically, normal thyroid tissue was found; others saw cystic colloid goiters, or rather, irregular thyroid tissue (Schilder, lit.). That it may function was proved in a number of cases in which the tumor was removed because it impeded speech and respiration, and when the thyroid was absent in its normal place, the extirpation caused myxedema (*e.g.*, cases of Berger, Getzowa, Lindt); in the case of Asch, parathyroids were demonstrated besides goiter, and their removal led to subsequent tetany (in ref. to myxedema and tetany, see p. 526). See Rubeti for lingual struma as a dangerous complication of pregnancy.

A most extraordinary case is that of a 50 year old woman showing a struma the size of a hazel nut at the tip of the tongue, reported by Goris, a proof that the medial anlage of the thyroid gland may advance as far as the tip of the tongue (Erdheim).

In the vicinity of the foramen cecum of the tongue are also found peculiar benign tumors, often small-cystic, consisting of various forms of epithelium, occurring in the presence of complete or unilateral aplasia of the thyroid (Aschoff, Erdheim, the author and Dieterle, Ungermann, Schilder, lit.). As Meixner emphasized, they probably belong to the goiters of the base of the tongue, especially because of their possible vicarious activity. These are tumors of the lingual duct, and Schilder (lit.) suggests that the strumas of the lingual base should all be thus designated. Wagner described a case in which there was no thyroid aplasia, but the epithelial tumor showed malignant properties.

Literature of goiter of the base of the tongue and related matter in appendix.

So-called cylindromas (comp. p. 182 and under gums) occur occasionally in the floor and elsewhere in the mouth cavity.

### Malignant Tumors of Soft Tissues

**Carcinoma.**—Carcinoma of the structures of the mouth is frequent, occurring chiefly in the lips, the tongue, the mucosa of the cheeks, more rarely in other parts.

Carcinoma of the lips, much more frequent on the lower lip, is a squamous cell tumor, the majority with marked tendency to cornification. It sometimes grows slowly, is hard and dry, in other cases, medullary; it

cornifies but slightly or not at all and grows quickly. Sooner or later the regional lymph nodes are involved.

According to the author's data, in 98 carcinomas of the lip, 73 occurred on the lower lip.

It is more common in males between 50 and 70 years of age. In the 98 cases, 75 were in males (lower lip 57, upper lip 18), 23 in women (lower lip 19, upper lip 4). It is generally considered related to smoking (pipe, see Broders). Strasser described a carcinoma in a 35 year old man considered traumatic due to a shell splinter injury of the lower lip.

FIG. 244.—Papillary carcinoma markedly cornified, of lower lip. The plugs pushing into the depth are met by reactive small cell infiltration. Man 55 years old (low power).

Symmetrical carcinomas have been observed on both lower and upper lips; this has been considered evidence of direct transmission, but there are lymph vessel communications.

Carcinoma of the lip occurs in various forms:

It begins very frequently as a small, flat nodule on the border of the red of the lip and the mucosa, often between the angle of the mouth and the middle of the lip. This nodule then ulcerates, with more tendency to peripheral than downward extension. The growing tumor excites a reactive small cell infiltration (lymphocytes, leucocytes, eosinophiles, plasma cells, rarely giant cells). It is disputed whether or not the degree of reaction can be viewed as a measure of malignancy (v. Bartkiewicz). The tendency to infiltration of regional lymph nodes is slight. The carcinoma is often markedly cornified.

The tumor begins as a nodular infiltration in the depth of the lip, which feels firm to palpation; the thickened lip is tensely stretched. (In a lower lip, removed for carcinoma, and tensely stretched and hard during life,

the author found, instead of the carcinoma, a cysticercus cyst larger than a pea. In a man of 53 years a varix the size of a pepper corn had clinically been interpreted as carcinoma. It was situated in the depth of the lower lip near the red part.)

The tumor tissue on section is white, medullary, sometimes almost poultaceous; the tumor plugs are often so large that on cross section they produce a macroscopic alveolar etching. Sections made by the freezing microtome disintegrate when placed in water. Ordinary sections show marked small cell infiltration of the connective tissue around the carcinoma plugs, and if the tumor is a cornifying squamous cell carcinoma, many so-called pearls are seen (illustr. under skin). Other forms show no cornification. When the infiltration softens, the resulting ulcer is of considerable depth, often crateriform, hard, thickened, with overhanging edges, blue-white in color from thick layers of keratosed pavement epithelium. The ulcer base is hard and uneven, sometimes roughly granular. The submaxillary lymph nodes are infiltrated early.

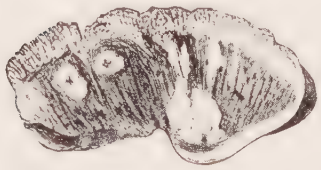


FIG. 245.—Carcinoma of tongue; perpendicular section through anterior end. Above in illustr. a flat carcinomatous ulcer, below this in musculature of tongue two sharply circumscribed carcinoma nodules with softened centers; to the left, a diffuse carcinomatous infiltration. In several places, white carcinoma strands descend from the surface; nat. size.

Another type develops from a hard papilloma, a horny papillary wart, the base of which becomes hard; it has a marked tendency to cornification and grows slowly; if ulcerated, the margins of the flat ulcer are hard and warty and the base covered with crusts. Without ulceration it is often difficult to differentiate from common verruca dura without careful microcopic examination of the tumor base (fig. 244).

In the differential diagnosis in situ, it is important to remember in ulcerated squamous cell carcinoma that cornified plugs, undergoing fatty degeneration or detachment by peripheral infiltration of cells, can be pressed out of the base of the ulcer like comedos. In view of the frequency of secondary syphilitic manifestations (papules), the position of the carcinomatous ulcer, between the angle of the mouth and center of the lip, is contrasted by the papules, usually in the angles of the mouth. Differentiation from hard chancre is usually possible by the more acute and extensive inflammation and the bacony infiltration of the latter; also the surface of an ulcerating chancre is rarely as papilliferous as a carcinomatous ulcer.

A tumor, clinically carcinoma, located in the lower lip of a man 56 years old, was found by the author to be a plasmacytoma (p. 272). Teleangiectatic granulomas (see under skin and p. 564) may be mistaken for carcinoma.

Carcinoma of the tongue, its most frequent neoplasm, starts from the epithelium of the mucosa as a markedly cornifying squamous cell tumor. Occasionally it arises from the glands of the lingual mucosa. They begin as small cartilage-like elevations similar to hard chancres, or as white warty excrescences, indurated at their bases, or as red flat nodules with ulceration, or as excoriations or tears or vesicles which rupture, leaving excoriations or ulcers. Very soon a superficial ulcer or a nodule is developed favoring the lingual margins. The ulcer grows relatively slowly, but the nodule may be followed quickly by medullary infiltration within (infiltrating form); if these infiltrations soften and rupture, they leave crateriform

FIG. 246.—Leucoplakia carcinoma of tongue. Cornifying squamous cell carcinoma on the base of lingual psoriasis existing for 25 years in 71 year old man, constant smoker, not syphilitic; to left, leucoplakia, to right, carcinoma; location back of tongue. Patient had no recurrence up to his death (77). (Low power.)

ulcers and depressions. Both forms can be combined with papillary proliferation. The ulcers have hard margins and bases, and the comedo plugs mentioned above can be squeezed out.

Carcinoma of the tongue also favors males; its development has been blamed on smoking, with the idea in mind that tobacco juice, like other substances, such as tar and paraffin, is an irritant leading finally to carcinoma. About 15% occur in women, relatively often in younger individuals (comp. Gorse and Dupaich).

In 91 personal observations of the author, 29 occurred in women; the highest number, 9, in the seventh decade; 4 occurred in the third decade.

Mechanical irritations are also alleged responsible factors, such as chronic friction and excoriations from carious stumps of teeth, and thus mostly for those arising on the lateral margins. In the 91 carcinomas of

the tongue, the author met this combination 7 times, and he saw it in quite young women (26 to 37). Leucoplakia oris (p. 553) is a frequent starting point, according to v. Bergmann (cited by Kuttner); 34.6% of carcinomas of the tongue developed in leucoplakias. Sometimes areas of previous primary syphilis become points of origin; lues itself is said to be a predisposing cause (Power). In rats infected with spiroptera neoplastica, Fibiger saw carcinoma develop in a glossitis in a few cases. In reference to leucoplakia carcinomas, Reclus emphasizes their relatively benign character in most cases, infrequently attacking the lymph nodes and not recurring after removal, in situ, but on the other hand, they reappear

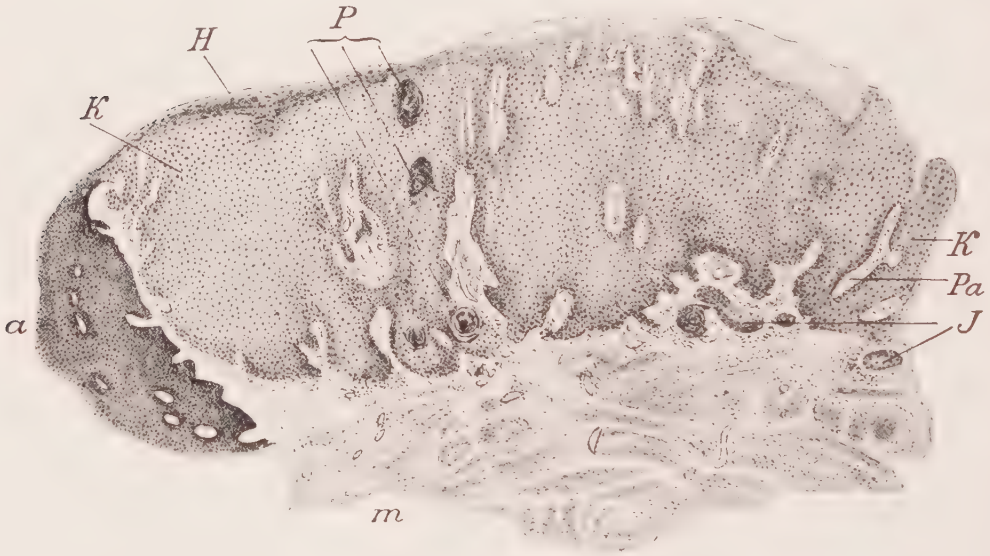



FIG. 247.—Squamous cell carcinoma of tongue; portion of edge. a, normal epithelial covering (papillae cut across); below musculature m, with vessels; above K, connected growth of carcinoma tissue (squamous epithelium with some epithelial pearls P) into which project cellular, vascular, large and branching papillae (Pa) of the mucosa. Below the large massive carcinoma, four apparently isolated carcinoma plugs (J) in the cellular mucosa; H, cornified topmost layer of carcinoma; about × 18. Tumor from margin of tongue of a woman 37 years of age.

rather frequently in other areas, often quite distant, as the tongue or the mucosa of the cheeks (comp. the case illustrated, fig. 246).

According to Konig, lingual carcinoma runs a quick course, at the most lasting 1 to 1½ years; it is characterized by great pain and horrible destruction (fig. 248). (Statement in 1881, but there has been little change. All of Dollinger's operated cases died during the next two years, Internat. Chirurg-Kongr., Brussels, Sept., 1908.) Butlin's statements are more favorable. The author's prognosis is a trifle more favorable, at least, in leucoplakia carcinomas (comp. Riedel; Ehrlich). The tongue is quickly infiltrated to a great extent, ulcerated and fixed to the floor of the

mouth. The jaw, the soft parts of the mouth, the salivary glands, the palate, regional lymph nodes (submaxillary, submental, deep cervical, more rarely, the supraclavicular bilateral; Kuttner) are quickly involved; in some cases, they are small, hard, painless, in others voluminous, soft, tending to disintegrate. Not rarely, the suppurating carcinoma with its tendency to hemorrhage ruptures externally. Metastases to distant organs are not frequent; death is due to cachexia, suffocation (edema of glottis) or aspiration pneumonia (gangrene).

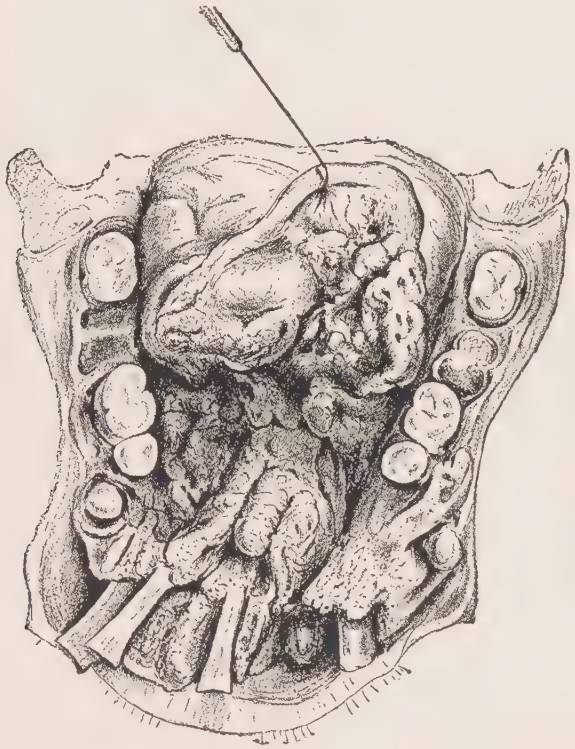


FIG. 248.—Extensive carcinomatous destruction of the floor of the mouth, the lower excavated part of the tongue (point lifted up) and the alveolar process; 9/10 nat. size.

In very old individuals, in spite of several local recurrences, the author saw relatively favorable results, *e.g.*, in an 80 year old woman, first operation 3½ years before, local recurrence, and 3 months later a second recurrence.

Both secondary hematogenous and lymphogenous metastatic carcinoma of the tongue is rare from distant organs. In a 52 year old woman with a cervical carcinoma, metastatic to the thoracic duct, the author found continuous retrograde extension through the lymphatics and a carcinoma nodule in the tip of the tongue (described by Winkler).

Carcinoma of the mucosa of the cheeks, beginning as a shallow, checkered ulcer with hard margins, sometimes originates in a leucoplakia or an active syphilid or in a syphilitic scar; as a whole, they are perhaps more frequent in luetics (Letulle). The folds are favored, such as in front of the ascending ramus of the lower jaw, in the depths of the cheek pouch, alongside the horizontal part of the lower jaw (Kuttner). The course is usually rapid. In the differential diagnosis, leucoplakia and tuberculosis must be considered.

The buyo cheek carcinoma is frequent in the Philippines in those who chew a mixture consisting of piper betle, betel nut, glue and tobacco; this is an example quoted for the irritation theory of carcinoma (Davis).

Carcinoma of the gums is rare; the tumor is flat and ulcerated, or nodular, often of slow growth (carcinomatous epulis described below).

Carcinomas of the floor of the mouth are squamous cell tumors of the mucosa or cylindrical cell growths from the submaxillary glands; they are rare, show a tendency to marked ulceration and spread to the tongue, jaw and lymph nodes.

For differential diagnosis, see tuberculosis (p. 555), hard chancre (p. 557), gumma (p. 556), actinomycosis (p. 558), local amyloid (p. 564) and carcinoma of the lips.

**Sarcoma.**—Sarcoma of the soft structures of the mouth cavity, especially the tongue, is very rare.

We may differentiate an interstitial and a tuberous, sometimes pendulous form of lingual sarcoma. It appears at any age (Baastrup). The starting point is intraglossal or submucous. Hemorrhage and pain are rare. See Naegeli (lit.) in reference to lingual sarcoma in childhood. The author saw a spindle cell sarcoma with slightly fibrous interstitial tissue noticed soon after birth, on the dorsal side of the tongue of a 5 months old baby. The usual types are round and spindle cell tumors. The author saw a hemangiosarcoma as large as a cherry on the base of the tongue of a 7 year old girl and a hard tuberous fibrosarcoma the size of a hen's egg, with a smooth surface, on the back of the tongue of a man 83 years of age; it had invaded the epiglottis; a man 39 years old developed a large round cell sarcoma of the floor of the mouth. According to Betke (lit.), who described a spindle cell sarcoma with isolated giant cells, in a man 83 years old, there are only 41 cases in the literature. Barth reported a lymphangiosarcoma of the floor of the mouth, and Schleinzer (lit.) one of the tongue. See also Blanc.

Rhabdomyomas of the tongue are very rare (Pendl, Richter).

On the other hand, certain sarcomas are frequent in the gums; they spring from the periosteum or the bone marrow of the jaw, and belong to the group of tumors called "epuli" (from the Greek meaning "gums").

Virchow used the word "epulis" only in its topographic sense; the term included tumors of various derivation and merely meant a tumor situated on the gums, but the name was extended to include tumors of the alveolar processes, alongside of the teeth or in gaps between teeth, and thus only displace the gums.

The designation fibrosarcomatous epulis is used, *e.g.*, in a 23 year old man; the author saw one as large as a hazel nut, and one the size of an almond in a man of 30, both periosteal; the prefixes myxomatous, osteofibromatous, hemangiofibromatous, etc., are added as the case may be. But carcinoma of the gums is not called an epulis; on the other hand, a carcinomatous epulis is a tumor which originates, *e.g.*, from epithelial rests in the periodontium (see p. 591).

The author saw epuli in a woman of 30 and in one of 34 years of age which corresponded to the plasmacytoma (p. 272); see case of Pirone and comp. p. 564.

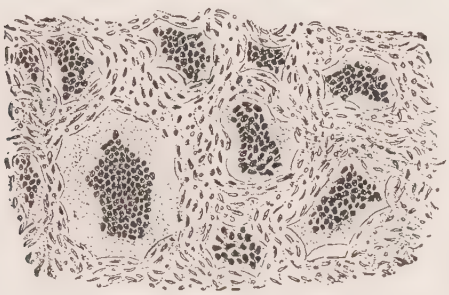


FIG. 249.

FIG. 250.

FIG. 249.—Epulis (sarcomatous) giant cell from periosteum of superior maxilla. Giant cells with numerous nuclei situated between spindle cells and fibrillar interstitial substance; clefts around some, probably due to retraction during hardening. (Medium magn.).

FIG. 250.—Giant cell epulis (sarcomatous) of the upper alveolar process from an anemic 9 year old boy. The tumor (E) grew very quickly and was blue red in vivo; S, mucosa and gums; A, alveolar process, i.e., a piece of its anterior wall removed by chisel followed by cauterization with hot point; nat. size.

When the surgeon speaks of epulis, he means the giant cell sarcomatous epulis (fig. 249) which corresponds histologically to a spindle cell sarcoma with an admixture of numerous giant cells. This is the classic type from which arise transitions to less cellular fibrosarcomas, often showing embedded newly formed bone spicules (fibroosteosarcoma).

In spite of its sarcomatous structure, this epulis is benign as a rule, because the most important property of a malignant tumor is absent, *i.e.*, the power to infiltrate tissues, to invade lymph nodes and produce metastases. But it does have a tendency to recur unless extirpated completely from the healthy bone or with the alveolar processes.

Other maxillary sarcomas, especially the round or spindle cell types and mixed tumors with sarcomatous elements, are malignant, some

extremely so (Hochenegg) with very poor prognoses (see under solid maxillary tumors, p. 593).

In some cases, the epulis rises as a broad based, smooth, rounded, rarely large tumor (periosteal form), attached to the bone, mostly the size of a pea to a hazel nut; occasionally the tumor is pedunculated. The consistency is soft or firm, color blue red, sometimes with a tint of brown granular blood pigment, which is more obvious in sections. If the tumor tissue arises within the bone (myelogenous form) it grows around the teeth, lifts them up, loosens them, and they fall out. Larger epuli are lumpy and lobulated, break through the mucosa and ulcerate or suppurate. The typical epulis appears at any time throughout life, perhaps somewhat more frequently in youth.

Many believe in an inflammatory origin from a carious tooth, etc., (Konig, etc.), which is quite correct in some of the cases. Haasler found close relationships between epuli and dental root granulomas (p. 586), often an identical architecture. Ritter believes in inflammatory and necrotic changes in dental roots as irritants to the periosteum (teeth, pp. 585 and 586), and he does not consider the giant cells as independent myelogenous, periosteal or endothelial structures, but sprouts, processes or buds of blood vessels (Wegner); he also believes the spindle cells are derived from vascular tissue. v. Recklinghausen, on the other hand, sees in a giant cell epulis "the highest stage of fibro-osseous new growth" (details in chapter on bone under fibrous ostitis); Stumpf shares this opinion. The author saw cases in which the morphological similarity was undeniable to fibrous ostitis and the giant cell sarcoma-like formations—brown tumors—of this disease (Lotsch).

Peculiar congenital epuli of perithelioma-like structure are very rare tumors around the upper incisors (Futh).

**Sublingual and Lingual Cystic Structures.**—Ranula, (from a superficial resemblance to the air bladder of frogs), in its classic sense, is a cystic tumor below the tongue in the free floor of the mouth, unilateral, bordered by the frenum where it is first noticed. It is globular or oval, without capsule and may reach the size of a mandarin orange. It has a blue appearance through the stretched oral mucosa, like a water filled bladder. The contents are as viscid as egg albumen, or thin yellow, red or brown.

There are three opinions as to its origin.

1. According to E. Neumann, a ranula is an enlargement of Bochdalec's tubes of the root of the tongue which have their origin from the thyreoglossal duct (p. 507), which also sends prolongations in the tissues under the tongue. These cysts are lined with ciliated epithelium, resting on polygonal (round—angular) epithelium.

2. Suzanne and R. v. Hippel have shown that clinically, outspoken ranula cysts may originate from the sublingual gland (Bartholin's duct), and Suzanne considers the gland acini, while v. Hippel thinks the small efferent ducts (duct of Rivini) are the starting points of the cyst formation. But these cysts have no true epithelial lining, but round cells, slightly flattened at the contact surfaces, and with swollen glassy protoplasm. This conception, shared by Sultan, satisfactorily explains the occasional development of a submental prolongation of the ranula, when this perforates the soft tissues of the floor of the mouth, usually at the lateral edge of the mylo-hyoid muscle, and proceeds downward below the chin to the neck.

3. v. Recklinghausen considers the ranula a retention cyst, due to occlusion and dilatation of a main duct of the Blandin-Nuhn mucous gland, situated at the tip of the tongue. The occlusion is said to be caused by inflammatory sclerosis of surrounding connective tissue, or blocking of the duct. The lining is of ciliated epithelial cells as in No. 1, although the gland in the tip of the tongue normally has no ciliated epithelium. This assumption of metamorphosis of non-ciliated into ciliated epithelium prompts E. Neumann and others to question the validity of v. Recklinghausen's conception. E. Neumann believes that the case investigated by v. Recklinghausen, which led to this theory, might be explained by errors in Bochdalek's tubes which Neumann has lately stated reach to the tip of the tongue.

Small cysts of the Blandin-Nuhn gland surely occur even congenitally (Foederl), but they occupy only the free tip of the tongue.

Wharton's duct (submaxillary gland) has nothing to do with ranula; its dilatation produces a cylindrical or ampulla-like cord which has no resemblance to a ranula.

See p. 507 in reference to small cysts of the base of the tongue, and those which occasionally are found in the line from the foramen cecum to the hyoid bone, with all or part ciliated epithelium, but having no macroscopic similarity to ranulae; their origins are from the thyreoglossal duct, or secondary glands attached to the duct, etc.

**Dermoid cysts,** or epidermoid cysts are usually solitary, median or fissural in the floor of the mouth cavity (sublingual dermoids) and may exceed a hen's egg in size. Lingual dermoid cysts are rare. They are filled with atheromatous debris, or with a tallow like, white substance, and lined with stratified pavement epithelium (similar to the epidermis). The smeary contents sometimes enclose hairs. In contradistinction to ranula, these cysts usually have a fairly thick capsule and are easily shelled out.

According to the development of the tumor toward the outside or the inside of the musculature of the floor of the mouth, distinction can be made between extra- and intraoral dermoids of the floor of the mouth.

As a rule both are firmly attached to the hyoid bone (Klapp). These dermoid cysts are considered due to epidermal inclusions (ectodermal rests; Hassel), or to invagination of skin during the time of formation of the mouth cavity. In the face, all situations in which there were clefts, may become the seat of dermoids; thus, *e.g.*, the orbital-nasal cleft, the inner and outer canthus, the root of the nose, etc.

Gill cleft cysts or branchiogenic cysts of the neck may push upward into the floor of the mouth cavity (p. 328).

**Appendix: Cystic Parasites.**—Cysticercus is quite rare (in the tongue, see Stumpf; in the lip, see observ. of the author, under lip). Echinococcus is somewhat less rare, and usually is tightly stretched so that no fluctuation can be detected.

## Diseases of the Teeth

Dental caries, the most frequent and important change in the teeth, and one of the most frequent diseases of mankind, is a progressive destruction of the enamel and dentine from without inward. The process consists, at first, of decalcification and softening, followed by solution and disintegration of the softened dental tissue. This double effect is essentially due to microorganisms (Miller), *i.e.*, it is a chemical-bacterial process.

Lactic acid is the first thought in decalcification; it is produced from carbohydrates (food residue) by the action of an enzyme of the saliva. Bacteria may also initiate acid fermentation in carbohydrate food remnants (Walkoff puts the onus on bread, see Seitz). Thirdly, there are bacteria, chiefly streptococci, bacillus necrodentalis and staphylococci (aureus and albus) which produce acids. These (lactic, acetic, butyric) formed in one way or the other, accomplish the decalcification and softening of the enamel and dentine, but complete solution of dentine is effected only by bacteria (dissolvers of dentine, Goodby). According to Miller, they supply a so-called peptonizing, but, according to Kantorowicz, a tryptic ferment and as aerobes thrive only on the surface and in easily accessible cavities. On the other hand, the organisms which enter and enlarge the dentine tubules are the facultative anaerobes, exclusively decalcifying, acid-forming streptococci, etc., mentioned above, with other obligate anaerobes of the group of butyric acid bacilli (Rodella).

Caries begins in the otherwise very resistant enamel membrane when it is penetrated and lifted off from the enamel by acid and bacteria; the enamel prisms are then loosened and superficially dissolved. Bacteria penetrate between the prisms to the dentine; acid-forming organisms, especially streptococci, enter the dentine tubules, dilate them and slowly dissolve the lime salts of the matrix. The clubbed thickened tubules become confluent, and the decalcified dentine is disintegrated and dissolved

by the ferments of other bacteria (for details in reference to the character of enamel, see Baumgartner; for dentine, see Kantorowicz; comp. Port and Euler).

Mechanical lesions (grinding, etc.) may also destroy enamel and create vulnerable points for caries. The softer the enamel, the easier and quicker the tooth is attacked. Blue-white teeth, teeth poorly calcified, and milk teeth are less resistant than yellow and permanent teeth. Growth, pregnancy and lactation, with their increased calcium requirements, favor caries (Williger). Another predisposing factor is rickets (p. 584); see Port and Euler, and critique by Kantorowicz in reference to the influences of civilization, food, etc. Caries may be brought about experimentally on extracted teeth, with a mixture of saliva, bread and meat in the incubator at 37°C. All the changes correspond perfectly to those of spontaneous caries. It is also observed on replanted or transplanted teeth.

The macroscopic beginning of caries consists of opaque, white, yellow to black brown spots on smooth surfaces; it begins most frequently in a furrow of the crown, on the contact surfaces, below the border of the enamel, as well as on the free surface of the tooth. In such places the enamel prisms are loosened and begin to undergo fragmentation. As soon as the softened enamel is dissolved, a defect is produced, a carious area, where the dentine is exposed; in this the softening and dissolving process continues until there are large cavities in the tooth. The enamel, far more resistant, is often undermined. The roots, especially of the molars, with their narrow pulp canal, not rarely remain intact. In these cavities innumerable bacteria and decaying food particles collect.

Caries of the neck of the tooth, chiefly on the labial or buccal side, is frequent in occupations dealing with sugar or flour which sticks on the free dental surface; for this reason "baker's caries" is spoken of (Port and Euler). Circular caries of the necks of the upper incisors, especially in the milk teeth, is said to be frequent in scrofula; H. Neumann made his diagnosis of scrofula in 36 among 60 cases from swollen lymph nodes, but Birkenhead thinks this latter condition was due in part only to caries, and Moro, who views caries of the neck of the tooth as a trophic disturbance caused by the lymphatism which prepares the ground for scrofula (p. 260), lately found no cutaneous reaction in 20% of the cases (p. 457). Escherich believes it is a result of a catarrh of the oral mucosa. Feiler thinks of a relation to rickets which causes a zonal weakening of enamel and dentine from within outward (p. 540). See M. Kraus in reference to occupation marks on teeth, partly from caries, partly from mechanical means, (in cobblers, upholsterers, glass blowers, tailors, etc.).

If the destruction in the crown progresses to the pulp (perforating caries), the pulpitis, partial or general, is accompanied by severe localized

toothache. The inflamed pulp, with its vessels and nerves, is swollen and red; it may suppurate and then the pain sometimes subsides.

Since the dentine tubules communicate with the pulp cavity, bacteria may enter before it is opened by caries, (Arkovy, Rothmann). More details by these authors in their atlas (Munich, 1903), also by G. Fischer and Landois.

When the inflammation descends into the root-canal, into the peridontium, the so-called root-membrane (its upper part is called "alveolar ligament"), and the space between the root and alveolus, the periosteum, rich in nerves, responds by a painful inflammation, which is naturally a peridentitis or periodontitis, or alveolar periostitis. Inflammation of the alveolar periosteum may be followed by complete necrosis of the tooth which becomes yellow and opaque, and frequently by a milder, or severe involvement of the maxilla with periostitis, ostitis, osteomyelitis and more or less extensive necrosis of the jaw.

FIG. 251.—Pulp granuloma in a carious ("hollow") lower molar; nat. size.

Severe lesions are relatively rare. Extensive necrosis of the maxilla is much more frequently (according to Graser) a consequence of acute osteomyelitis in measles, scarlet fever, smallpox, etc.

Alveolar pyorrhea is the term for a frequent chronic purulent inflammation in the periodontal space of the alveolar shelves, due to organisms and beginning mostly in middle life; spirochetae are also found, and are said to play an important part (Gerber, Turner, Seitz, Clemm); fusiform bacilli and buccal amebae are also present (W. Fischer). Tartar deposits possibly favor pyorrhea; diabetics are predisposed, heredity is important. In time, the teeth become loose because all the structures which hold them including the bony alveolar walls are destroyed by granulation tissue (Romer, Euler, Kranz; complete exposition by Port-Euler).

Pus may enter the marrow spaces of the alveolar processes, and from there spread to the outer maxillary periosteum, or along the neck of the tooth to produce a subperiosteal abscess, or "parulis," chiefly on the external side of the jaw. The gums are also inflamed, red, swollen, first hard, and later, if an abscess is developed (popularly known as ulcerating tooth), fluctuating. The pus is thick, green or discolored and usually foul smelling. The adjacent oral mucosa is swollen. The typical "swollen cheek" is due to inflammatory edema. Sometimes it is accompanied by high fever. The abscess subsides, or ruptures into the mouth cavity, after which the pain stops; if the diseased tooth and its root are removed, the abscess promptly heals, but if the root is allowed to remain, it causes a so-called dental fistula. Such fistulae lead into the mouth in the immediate vicinity of the tooth (internal or gum fistula) or the suppuration in

the maxillary periosteum and the soft tissues of the cheek perforates through the chin, or elsewhere on the lower jaw, in front or behind the ear, through the skin (external dental fistula). They are much less common in the upper jaw. Sometimes the pus burrows for considerable distances. Healing may result in deforming, deeply contracted scars. Relatively frequent and important is the relation of root periostitis of the second premolar, and the first and second molars to empyema of the antrum of Highmore (p. 296), although diseases of the latter are much more frequently of nasal origin. But granulomas from disintegration of the pulp develop fistulous openings into the antrum. Perforation of root abscesses into the nose or the orbits or the spheno-maxillary fossa are rare.

During the course of chronic periodontitis, ossifying inflammations and more active granulations appear on the periosteum of the root; the latter are discussed with tumors (p. 586). Pulp polyps or pulp granulomas are small red masses of granulation tissue, growing like buttons from the pulp exposed by caries (fig. 251), but they may resemble sarcomas or the granulomas of the root (p. 586). The bony root of the tooth (cement, osseous substance) and the alveolus may be rarefied and softened by the inflammation. This latter is true caries, as usually seen in bone, in contradistinction to dental caries causing destruction of the enamel and dentine, called simply "caries."

Further importance of diseases of the teeth, especially caries, for the organism, apart from the inability of perfect mastication and salivation of food, is the following:

(*a*) The accumulation of various microorganisms in carious teeth allows of the possibility of aspiration of bacterial plugs into the lungs with subsequent gangrene or abscesses. The same may be caused by aspirated fragments of carious teeth and they have been found repeatedly in gangrenous pulmonary foci.

(*b*) Dental caries as a frequent cause of swelling of lymph nodes in children, occurring first in the submental and easily palpable submaxillary nodes. Hollow teeth are probably less direct portals of entry to the lymph nodes, although Koerner considers the absorptive power of the pulp an important factor, while others emphasize the lack of lymph channels in carious teeth (Moeller), than indirect portals by making the mouth a veritable incubator for all kinds of bacteria from which they reach the lymphatics and lymph nodes (p. 258).

(*c*) Empyema of the antrum of Highmore of dental origin mentioned on p. 296.

(*d*) The presence of many carious teeth and pyorrhea might initiate anginas; and if bacteria enter the blood, general septic infections of various

kinds, such as articular rheumatism, exanthemata, etc., (Passler, M. Fischer). Such unhygienic mouth cavities in surgeons, midwives, etc., (Guttmann) may be a source of droplet infection (p. 456).

(*e*) According to some opinions, dental caries may be a portal of entry of actinomycosis, but this has been emphatically denied by von Baracz (p. 560 e.f.); the fact is that occasionally, according to Lord, even frequently, fungi can be found in carious teeth. Tubercle bacilli may reach the pulp and roots to cause tuberculosis of the maxilla (G. Fischer).

(*f*) Dental caries is the most important predisposing factor in the maxillary necrosis due to phosphorus poisoning (see under bones).

(*g*) Sepsis has followed periodontitis and parulis; extensive suppurating phlegmons occur in the mouth structures, or maxillary osteomyelitis. Death may supervene from aspiration pneumonia, edema of the glottis, meningitis from conduction of the process along the trigeminal nerve, etc.

FIGS. 252 and 253.—Marked formation of tartar on an upper molar, and a lower incisor (viewed laterally); nat. size.

Dental tartar consists of dead fungi, especially the leptothrix (p. 559), mucus, epithelium and food remnants which have become precipitated with calcium carbonate and calcium phosphate to form incrustations. It is soft, white, yellow, or harder, very firmly attached, green, brown to black. Tartar causes gingivitis; it may enter the alveolar process, forcing the gums away, giving rise to pyorrhea (p. 578), or alveolar atrophy with loosening of the tooth.

### Malformations and Tumors Related to the Teeth

**Embryology.** (Figs. 254 and 255.)—The epithelium of the mouth cavity and the mesoderm of the maxilla participate in the development of the teeth. A continuous strip proliferates from the epithelium of the maxillary margin obliquely into the underlying connective tissue; this strip is the dental anlage (enamel). From here, solid plugs corresponding to the number of milk teeth, grow outward and down into the mesoderm; these are the first anlage of the enamel producing organ which also determines the shape of the tooth. High cylindrical cells face the mesoderm, while within the plug are rounded epithelial cells. While the union of the enamel organ with the dental anlage is more and more reduced to the

thin core-shaped neck of the knob, and finally is completely separated by the mesoderm, the mesodermal dental papilla, which may be compared to a papilla of a mucosa, penetrates each knob from below.

The enamel organ, now larger and bell shaped, has three types of cells: the inner, single layer, high cylindrical enamel epithelium directly covering the mesodermal papilla, the outer epithelium of the enamel organ, in a wide arc running toward the neck of the knob, cubical and flatter in shape, and the cell substance in between, *i.e.*, the enamel pulp (s.p. in fig. 254), where the epithelium by the rapid increase of the fluid intercellular substance is changed into a so-called gelatinous tissue consisting of stellate anastomosing cells (fig. 258). On the base of the papilla the outer enamel epithelium passes over into the inner epithelium.

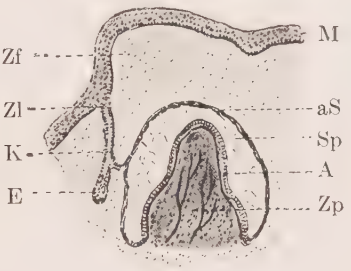



FIG. 254.—Development of tooth (diagram). M, buccal epithelium; Zf, gum; Zl, dental ridge; K, neck of knob; E, enamel for substitute tooth; Zp, dental papilla with vessels; A, adamantoblasts (inner enamel cells); Sp, enamel pulp; aS, outer enamel cells. 5 months old fetus.

Between the inner enamel cells and enamel pulp may still be distinguished a layer of closely packed epithelium, the so-called intermediary layer. Enamel (adamantine or vitreous substance, p. 582) is supplied only by the upper portion of the inner enamel epithelium (ameloblasts, adamantoblasts) which surrounds the future dental crown.

The epithelium of the lower rims of the knobs grows still more deeply into the mesoderm and is later placed (without the power to elaborate enamel) around the root of the tooth, forming v. Brunn's epithelial sheath of the dental root, and consisting of the directly superimposed outer and inner cells of the dental organ.

This sheath is slowly perforated by mesodermal cells and undergoes involution, but epithelial rests remain for life, as the so-called "debris epitheliaux paradentaires"—a sort of abortive dental germinal substance, —, which were found by Molassez in every adult examined by him, in the form of globular, cylindrical or oval collections or strands (Galippe). Some of the cells are polygonal, resembling the epithelium of the oral cavity; others are cylindrical. They are scattered from the epithelium of the gums to the ends of the roots in the peridontium surrounding

especially the roots. Partsch never saw the network arrangement in man as described in the cat by G. Fischer.

The surface of the young papilla is covered with palisades of high cells, the odontoblasts. These produce dentine, not by themselves, but, according to Mummery and v. Korff, with the help of numerous fine fibrillae which are gradually concentrated (substantia eburnea, the main body of the tooth); during its development the papilla gradually becomes pulp; its outer layer is formed by odontoblasts. Meanwhile, but not

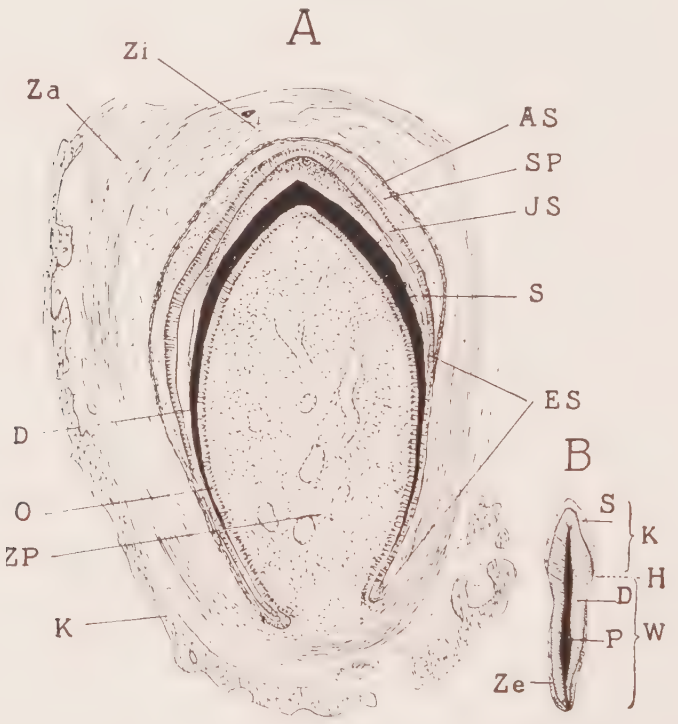



Fig. 255.—A and B. Fig. A. longitudinal section through young milk tooth (newborn) (after Stoehr). AS, outer enamel cells; SP, enamel pulp; JS, inner enamel cells; S, enamel; D, dentine (black); ES, epithelial sheath v. Brunns; ZP, dental papilla with vessels (later pulp); O, odontoblasts; Za, dental capsule, outer; Zi, inner layer; K, bone of jaw. Fig. B. Cross section through an incisor; S, enamel, D, dentine, P, pulpa (black); Z, cement; K, crown; H, neck; W, root.

until dentine has been deposited, the inner enamel cells have formed layers of enamel, consisting of hexagonal prisms and interstitial substance, at first soft, later hard from progressive calcification (details by Schaffer). These enamel layers cover the dentine on top (black in fig. 255), (beginning of the crown of the tooth).

The enamel organ, papilla and the young tooth are then surrounded by connective tissue fibres, forming the dental sac or follicle (about the 20th

week) which surrounds the whole dental anlage; later the follicle consists of an inner loose (Zi) and an outer fibrous layer (Za); it produces the cement substance which is rich in Sharpey's fibres, penetrating it from the maxilla and passing through the periosteum. The alveolar periosteum or the root membrane, rich in nerves, fills the space between root and alveolus (p. 578); its upper part is called alveolar ligament or circular dental ligament, and consists of firm bundles of connective tissue, closely united to the gums (gingiva).

There then occurs the eruption of the first (20) milk or decidual teeth (8 incisors, 4 canines, 8 molars); the root lifts the tooth upward, its apex breaks the epithelial covering, *i.e.*, the remnant of the enamel organ, and is forced through the gums; these tissues undergo pressure atrophy. In the 6th to 8th month the lower incisors appear, first the median, then the lateral, etc.; at the end of the 2nd year, the eruption of all milk teeth is complete. The anlage for the permanent teeth is again at the epithelial dental ridge; even as early as the 3rd embryonal month, close to the neck of the bulb of the milk tooth, there appears a prolongation of the epithelial ridge into the mesoderm which begins the secondary enamel anlage for the permanent teeth. These enamel anlage lie at first in the alveoli of the milk teeth and labial, but later they receive their own alveoli. At birth, the anlage of the permanent incisors and canines have a dental sac. The permanent tooth lies below the milk tooth, separated from its root by the alveolar wall. The 32 permanent teeth (in each jaw, 4 incisors, 2 canines, 4 premolars, 6 molars) develop exactly in the same manner as the milk teeth. During the change the separating alveolar wall and the roots of the milk teeth become absorbed by the pressure exerted by the erupting permanent teeth and osteoblasts (some giant cells); this absorption progresses even into the enamel. Occasionally osteoblasts separate the tips of the roots and absorption follows later. The milk tooth thus loosened, is forced upward until it drops out. This replacement commences in the 6th year with the 1st molar; in the 7th year there follow the lower and upper median, in the 8th year, the lateral incisors, in the 9th, the 1st premolar in the upper and lower jaw, in the 10th, the 2nd premolars or the canines, in the 11th, the canines (or the 2nd premolars), in the 12th, the 2nd molars. In the 12th year dentition is almost completed with the eruption of 28 teeth; four wisdom teeth are lacking. These last molars of each jaw appear between the 16th to 40th years or never appear; their eruption may be accompanied by maxillary periostitis and phlegmons of the neck. Exceptionally, change of teeth may be repeated 2 to 6 times during youth, and perhaps the very rare 3rd dentition may occur in advanced age (G. Fischer, good table in reference to the phase of dental growth).

These rather complicated processes explain:

**Developmental** disturbances and malformations of teeth (details and lit. by Peckert, Broman). Among other conditions, rudimentary teeth, without enamel, *i.e.*, consisting only of dentine and cement, absence of some teeth, most frequently the wisdom teeth, lateral upper incisors; smaller numbers often considerable, quite the rule in so-called hairy men, although hypotrichea and its highest degree anodontia, are rare (Wieting and v. Moos, lit.); excess of growth, giant growth, and excess of numbers where the dental ridge is more furrowed by the mesoderm and causes new anlage; instead of one large tooth, several smaller teeth may appear. There are also twin teeth, union of a normal and one or two supernumerary teeth anlage; adhesion of teeth is due to cement hypertrophy at the roots of two separate teeth; fused teeth are two normal primitive teeth fused together in their early soft stage,—kinking and torsion is relatively frequent, making normal extraction impossible, also excess and lack of numbers and growing together of dental roots. Accessory teeth, as canines of the superior maxilla, dislocations, heterotopics are seen, *e.g.*, the presence of two teeth superimposed, or an incisor in the nose, orbit, antrum of Highmore, or a molar on the hard palate, which may be due to aberrant processes of the dental ridge. See under skin in reference to Hutchinson's teeth in congenital lues, also in reference to pseudo-Hutchinson's teeth, caused by unilateral wear. The changes of rickets are also manifold, among others, marked delay in dental formation and late eruption, disturbed calcification of dentin; the teeth are soft and fracture easily, as observed by Erdheim in analogous manner in rats with parathyroids removed (p. 539). According to the opinion of some authors, enamel hypoplasia also occurs.

"Erosions" or hypoplasia of the enamel consists of a defect in the enamel on some small area, usually horizontal, or entire absence of the enamel exposing the dentine. At present it is generally denied that lues is especially active in its occurrence (Neumann); the same may be said of rickets (Fleischmann). Indeed, all enamel hypoplasias are supposed to be a consequence of tetany (in which other epithelial structures, such as the nails, hair, lens, are influenced), *i.e.*, the basic changes are in the parathyroids (Fleischmann). (More details in relation to organs of internal secretions by Josefson; thymus and hypophysis are supposed to control the growth of teeth; Kranz, elimination of these glands causes hypoplasia of growing teeth, premature atrophy of the thymus causes loss of all teeth.)

**Tumors** of various types may arise from actual dental anlage (epithelial enamel organ, mesodermal papilla with odontoblasts), or from its coverings (dental sac, cement, alveolar periosteum); the tumors are of both epithe-

lial and connective tissue nature, and some tumor-like new growths are composed of specific dental substances (enamel and dentine). To true tumors are added tumor-like tissue malformations, and proliferations (granulomas) of various composition, which in their turn, may become the starting point of true tumors. This conception explains the manifold formations under question. A great number of the solid and cystic maxillary tumors can be considered derived from the dental system. There may be mentioned:

Enamel droplets (emailloids, adamantomas) are small congenital thickenings consisting of enamel, more exactly, of a dentine body with enamel covering, located usually where the enamel stops and the cement begins, *i.e.*, at the transition of crown and root. Some think they are derived from the primary osteoblastic inversions which supply the dentine body, while the enamel is supplied by the epithelial sheath of the enamel organ (Walkoff, Kantorowicz); others consider them diverticuli of enamel anlage (lit. by Peckert).

Certain rare benign epithelial tumors are called adamantinomas; the rarer ones are solid, fairly soft and slow growing tumors which may, however, become focally liquefied from vacuolar degeneration; stellate epithelium is found similar to that of the enamel pulp (fig. 258); others are cystic, being composed of smaller and larger cysts. These tumors may reach the size of a fist, are usually well encapsulated, lie in the maxilla which becomes distended like shell; more rarely they are polypoid proliferations at the edge of the gums. (More details under so-called multilocular maxillary cystoma, p. 589.)

Odontomas, relatively rare tumors, consist of dental substance springing from a normally situated or heterotopic or extra anlage; in the beginning, and sometimes permanently soft, they are called myxomas, fibromas, fibroplastic tumors (Dupuytren, Magitot), or better, merely soft odontomas, in which pulp tissue and peridontium predominate, *i.e.*, soft dental tissues; increasing amounts of dentin, produced by odontoblasts or enamel or cement, produce the more frequent hard odontomas favoring the vicinity of the wisdom teeth, and finally remaining stationary (Virchow). Older terms emphasize the predominance of one or the other dental tissue elements, as: dentinoids, adamantine odontomas, osteo-odontoma, etc. Odontomas may attain considerable size (hen's egg and more, with a weight of more than a kilogram) and distend the maxilla. They favor the lower jaw. (Lit. by Schumann, Schloessmann, Perthes, Leriche and Cotte, Peckert.)

Dentin is deposited in the pulp during the period of use, and may gradually narrow the pulp cavity, *i.e.*, the canals. According to Reich, irregular dentin is distinguished by kinking and torsions of the canaliculi, etc. Protective, or substitution dentin is laid down to cover the wear,

especially of the molars and premolars by mastication; thus the grinding surfaces, the walls and the roof of the pulp cavity are thickened; it is also deposited in carious teeth and under dental fillings. Small, globular, tumor-like denticles may form in the pulp itself as free bodies or fused to the walls. According to G. Fischer and Landois, their origins are from embryonal inclusions and as responses to physiological stimuli which cause pulp cells to become differentiated into osteoblasts supplying dentine and also papillae.

Dental osteomas (Virchow) arising from the cement are called dental exostoses if circumscribed, dental hyperostoses if diffuse; they are small tumors or thick coatings on roots of diseased teeth.

Pulp granulomas are described on p. 579.

Root granulomas are very frequent, small, fleshy structures firmly attached to the roots, usually at the tips, coming from the alveolar ligament (p. 583) and due to an inflammatory proliferation of preexisting tissue. They are differentiated into those which contain epithelium, and those which do not. In the former, the so-called epithelial granulomas (Romer), there are found granulation tissue, the vessels of which show active endothelial proliferation, fibrous tissue with degenerative changes, especially fatty and mucoid giant cells (as in epuli, p. 573), mixed bacterial flora, leucocytes, and many plasma cells (Dreuw and Rumpel), showing various peculiar degenerations. Of especial interest are epithelial inclusions, *i.e.*, remnants of the epithelial sheath (p. 581), usually in the form of strands of flattened, cubical, or low cylindrical cells (Haasler), most markedly developed in the vicinity of the ends of the roots. In the capillary loops growing through the proliferating epithelial masses are peculiar figures, called "epithelial bells" by Romer, plugs of connective tissue, liquefied in time and covered with epithelium. These granulomas recede or become the starting point of true root tumors of the connective tissue (p. 592, solid maxillary tumors) or epithelial, or mixed connective tissue epithelial groups, some solid and some cystic.

**Maxillary Cysts and Cystic Tumors of the Maxilla.**—We may differentiate:

(*a*) Dental cysts which are classified as:

(1) Simple or follicular dental cysts (follicular maxillary cysts of Magitot), rare.

(2) Dental root cysts or cystic root granulomas (periosteal maxillary cysts of Magitot, peridontal cysts, dental root cysts), frequent.

(*b*) So-called multilocular cystomas or polycystomas, better, cystic adamantine epitheliomas or polycystic adamantinomas, a true neoplasm.

The cysts (2) favor the upper jaw; the cysts (1) are more frequent in the lower jaw. The cysts (*b*) favor the lower jaw. Those in the superior

maxilla are twice as frequent. The cysts (2) spring only from diseased teeth (Partsch).

(1) They arise from a dental anlage, normal or abnormally placed, normal or supernumerary; they are really miscarried, cystic malformations.

According to Malassez, they do not grow from a dental follicle, but from aberrant epithelial buds, or remnants of the epithelial sheath. See Perthes against this view; perhaps both are correct.

The position of these cysts is variable; they are found not merely in every part of the maxilla, but also in the gums and rarely in the orbits. Probably they never reach the size of polycystomas, but may become as large as a hen's egg. As a rule, they are lined with pavement epithelium, but may exceptionally have a cylindrical epithelial lining; they are unilocular. They usually are noticed toward the end of the dental change (Peckert), but often require many years to reach a fair size. The cavities contain a serous, sero-mucous, or sero-sanguinous fluid with fatty degenerated cells and cholesterin crystals, perhaps also rudiments of teeth, or misshapen, but otherwise always perfectly healthy teeth, rarely in great numbers, but Hildebrand found 150 teeth in one cyst. Sometimes cystic degeneration of a normal or supernumerary dental anlage (dental sac with its contents, so-called follicle) prevents the development of a tooth, although this is not always the case; more frequently a tooth, absent in the set, is found with the crown turned towards the cyst; perhaps, however, it is only a rudiment. If the cyst contains numerous teeth, the supposition is that multiple supernumerary dental anlage were present.

(2) Root-cysts are the result of periostitis of the root, but while it was formerly assumed that the root periosteum was lifted off by pus (Magitot), later investigations have shown a close relationship to root granulomas, *i.e.*, the "epithelial granulomas" (p. 586). Middle life and the superior maxilla are favored.

Larger cysts, clinically important, grow slowly and are rather rare; small ones are quite frequent. According to Partsch and Haasler, internal liquefaction with cavity formation takes place in the granuloma, while the outer portions change into a firm fibrous mass which constitutes the cyst wall. Flattened epithelium, sometimes in 3 to 4 layers, more rarely cubical, low or high cylindrical, lines the cavities. In reference to the epithelium, cysts (1) and (2) do not differ from each other; the cells are derived from Malassez's nests (see pp. 581 and 586). They may be lost if the cyst suppurates, and forms an abscess. According to Grawitz, suppurative liquefaction occurs in an apical inflammatory focus, originally free from epithelium, the abscess drains through a fistula in the destroyed alveolar wall into the mouth, and from there the epithelial lining of the

abscess cavity is started. But this explanation is not accepted by Partsch or Petersen, while G. Fischer and Landois support it.

If such a cyst is removed in toto, it is found to be a sack with a sort of a neck containing a diseased tooth, the roots of which reach into the sack. Its wall is formed by an outer fibrous, or middle cellular and vascular, and an inner epithelial layer; the details, however, vary. In places where there is tension, there is a thin, single epithelial layer over fibrous connective tissue; in other places, there are tiny warty collections of "epithelial bells" (p. 586), with the fibrous tissue still undergoing liquefaction and for this reason not yet ruptured. Partsch calls this the "germinal field" for the further development of the cyst. Sometimes, however, the wall shows microscopically a complicated system of epithelial cavities, a polycystoma in miniature.

These peridontal cysts may distend considerably in the upper jaw, and more or less fill the antrum. According to Zuckerkandl, they may be mistaken for empyemas, but according to Kuttner, more easily for hydrops of the antrum. The old cyst, as a rule, contains a perfectly sterile, clear, slimy or syrupy brown fluid, exfoliated epithelium and cholesterin crystals, but if suppurating, pus. Fistulae are quite rare.

Subsequent to abundant exfoliation and new formation of epithelium, the cyst may also contain laminated, mother of pearl-like masses like a dermoid (Mikulicz). A carcinoma may develop from the epithelium of older cysts. Cysts occur in the maxillary bones, and, as elsewhere in the skeleton, are caused by fibrous ostitis (lit. Lotsch); see p. 573 under epulis and chapter bones.

(*b*) The second main group of maxillary cysts are the so-called multilocular cystomas or polycystomas, better named, adamantinoma polycysticum or polycystic adamantine epithelioma. These many-chambered tumors consist of solid masses and thin, smooth-walled cavities of variable dimensions, with thin fluid or gelatinous contents; sometimes they distend the jaw enormously, especially externally, even to the size of a child's head. They select the lower jaw almost exclusively. As a rule, their course is exceedingly chronic (decades) and benign (lit. by Becker, Pincus, Krompecher). They are inseparably related to the solid adamantinomas, which are much rarer and favor the angle of the lower jaw (p. 585 and the dissertation below).

The age of those afflicted with adamantinomas fluctuates within wide boundaries, from the newborn to old age, but most are observed between the ages of 30 and 50 (lit. by Georgi).

A specimen at Breslau shows the left half of the lower jaw distended to the size of a small fist by a multilocular smooth-walled cystoma. The bone appears puffed, numerous small bulgings make it as transparent as

tissue paper, and it crackles like parchment; in other places, especially at the markedly distended outer side of the jaw, the bony shell is perforated and is closed only by the fibrous cyst wall and the periosteum (fig. 256).

The origin of enamel epithelium tumors or adamantinomas, solid as well as cystic, rare, benign epithelial neoplasms, is considered from: (*a*) supernumerary enamel-organs or the primitive enamel anlage of a miscarried dental follicle (Hesse), or dental anlage which sprout like glands and alveoli and afterwards distend into cysts (follicular cystadenoma, Falkson); (*b*) invagination of the epithelium of the mucosa of the mouth,

FIG. 256.—Polycystic adamantinoma of lower jaw; case mentioned below in text; longitudinal section; inner aspect of outer half; nat. size.

the evolution of which ends with specialization into enamel epithelium (Krompecher, v. Bakay, Kuru); (*c*) or the paradental enamel epithelial remains of Mallassez (p. 581). As Leriche and Cotte emphasize, these 3 theories are basically the same since the cellular material is originally from the same source. The 3rd theory has most followers and probably can be applied in the majority of cases. Conclusive observations, however, also support (*b*), as the author can verify on the basis of one case (solid adamantinoma of the lower jaw in a woman), in which some cell strands of the tumor were connected with the epithelium of the mouth. It is emphasized by some authors that these tumors are likely to follow diseases of the teeth, especially if remnants of roots remain; occasionally slight injuries give the impetus for their development (Hochenegg), but this latter should be viewed sceptically (v. Teubern). Microscopically, both the solid tumors, and the solid portions of cystic tumors, contain networks of

interwoven epithelial strands with sprout-like pocesses in the fibrillary connective tissue, rich in spindle cells (resembling the dental papilla); this suggests epithelioma or carcinoma columns and more faintly glands. But with careful study these epithelial bodies show a typical composition perfectly resembling an earlier or later embryonal phase of the enamel organs; thus, the outer cells are high cylindrical (corresponding to inner enamel cells), followed by flat or polygonal epithelial cells, which also form pearls, but without cornification, having hydropic degeneration within (corresponding to enamel pulp and characteristic of it), *i.e.*,

Fig. 257.—Polycystic adamantinoma of lower jaw; piece of more solid portion; a, fibrillary stroma rich in spindle cells; b, epithelial larger and smaller strands (spaces between a and b are artefacts). Strands on outside show cylindrical cells, otherwise polygonal and stellate cells. c, cavities caused by liquefaction of epithelial stellate cell masses; d, indication of concentric lamination. (med. magn.). (Macroscopic illustr. by Perthes, l.c., p. 457, fig. 50 and by Peckert, l.c., p. 457.)

intercellular fluid causing separation of the epithelial cells (fig. 258), in the nets of polygonal, stellate or branching cells. Further liquefaction of cell masses forms smaller or larger hollow spaces (fig. 257) which finally are cysts now surrounded only by cylindrical cells as in a gland. This type is the characteristic enamel pulp cyst. More colloid in the epithelium causes colloid cysts; then there are non-characteristic, lipoid or pseudo-xanthoma cell cysts, and finally cysts from granular disintegration of epithelium. Krompecher considers the adamantinoma a basalioma, more or less differentiated, but corresponding to a benign epithelioma. The tumor cells often contain much glycogen (Kuru, Georgi), especially the

clear marginal zones of the cylindrical cells. Occasionally papillary proliferations may grow into the cysts (Georgi, Josephy). The connective tissue is considered partly a constituent of the dental papilla, partly of the dental follicle (Joest). The rare predominantly or exclusively solid adamantinomas have been observed in the upper jaw in a few cases; they may invade the antrum of Highmore, or grow into the nasal cavity as soft masses (Stumpf, lit. Esch). There are also secondary, tooth-containing cystic adamantinomas, as in the case illustrated, fig. 257, of invasion of a second dentition tooth into the cyst cavity after absorption

FIG. 258.—Enamel epithelial plug showing hydropic degeneration within (similar to enamel pulp) causing the development of reticulum epithelium; outside fibrillar connective tissue. From a more solid portion of a cystic adamantinoma of lower jaw (high power).

of the cyst wall. The tooth is always solitary, and is usually well developed (Leriche and Cotte). Root cysts also may produce dainty polycystoma-like formation; comp. the microscopic findings, p. 587. Carcinomatous metamorphosis is occasionally seen; thus, in a case of the author, a benign cystic tumor was incompletely removed from the lower jaw; after some years there was recurrence with destructive character; the resected jaw showed cylindrical cell carcinoma with benign remnants of the cyst.

In cattle, there occur all transitions from simple adamantinomas, consisting simply of proliferation of undifferentiated enamel organs (without the formation of enamel) to tooth-like, hard growths consisting of dentine and enamel, called multidentiferous proliferating odontomas (Joest).

Some solid maxillary tumors are undoubtedly derived from the dental system (as mentioned, p. 585). They are classified into: (*a*) those of connective tissue, such as fibromas, pure or with epithelial inclusions and occasional transitions into sarcoma (lit. Blaud), myxomas, osteomas, osteo-

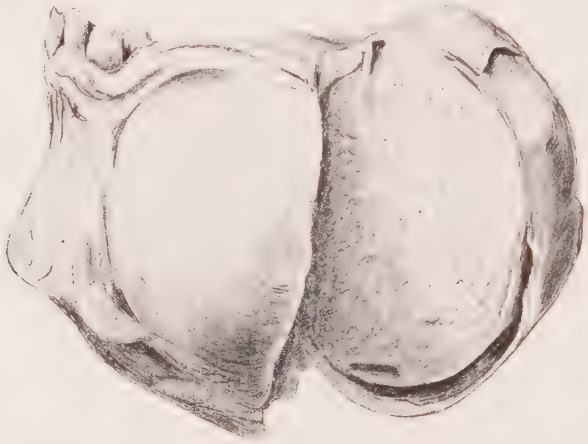


FIG. 259.—Central fibroma of the left half of lower jaw, with osseous shell; 7/8 nat. size.

fibromas (lit. Uyeno), sarcomas (round-, spindle- and spindle-cell giant cell), osteoid- and osteosarcomas, more rarely melanotic, mixed tumors, and combinations of these types; (*b*) epithelial (1) benign adamantinomas (p. 585), and (2) carcinomas, which are thought to be derived from

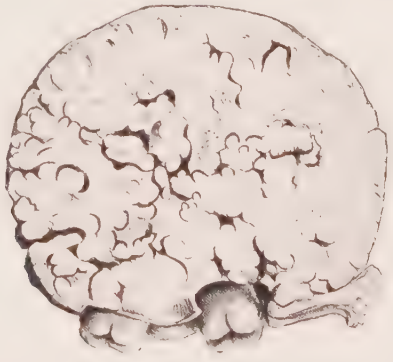


FIG. 260.—Osteochondrosarcoma of the right half of lower jaw, plexiform in structure; girl 26 years of age; 7/8 nat. size.

paradental epithelial rests, as far as they do not spring from epithelium of the mucosa.

Even melanotic carcinomas occur; Krompecher saw one which enclosed two teeth on the alveolar process of a 2 months old baby.

Maxillary tumors with the exception of carcinomas usually belong to the earlier part of life, and are small, hidden in the depths or presented

as prominent peripheral, partly periosteal tumors, and as epuli (see p. 572); central intermaxillary tumors distend the jaw to the size of a man's head.

It is noteworthy that metastases from carcinoma elsewhere also occur in the lower jaw, with paralysis (neuritis) of the alveolar nerve, as from carcinoma of the breast (H. Schlesinger). Schmorl saw carcinoma metastases in dental pulp.

(Lit. in reference to cysts, and solid maxillary tumors by M. B. Schmidt, Perthes; adamantinomas Erdheim, Bohmig, K. Fritsch, Hoffmann, Bautze, L'Esperance.)

### Diseases of the Salivary Glands

The parotid gland is the one most frequently diseased.

**Inflammation of the Parotid Gland. Parotitis.**—A primary and secondary parotitis may be differentiated:

(1) Primary, idiopathic parotitis, epidemic parotitis, catarrhal parotitis or mumps, appearing in epidemics or sporadically, is doubtless contagious; the most important symptom is usually bilateral, sometimes unilateral doughy swelling of the parotid and its vicinity, usually running a course of 1 to 1½ weeks and accompanied by slight fever.

The specific infectious organisms, bacilli of Charrin, Capitau and others, a small streptococcus of Busquet, Bein and Michaelis, a Gram-positive micrococcus tetragenus of Luschi, Merelli, easily cultivated from the blood, secretion of the salivary glands and hydrocele fluid, presumably enter Stenson's duct from the mouth, but the cause has not been verified. By injection of filtered saliva, Wollstein (lit.) produced inflammation of the parotid and testes in cats; others believe that mumps is a septicemic process with a special tendency of the organisms to locate in the salivary glands and genital organs (Merelli). Children and young adults are predisposed, boys preferred. Babies and old individuals are almost never attacked.

Occasionally the left parotid is involved alone or to greater degree. Sometimes the submaxillary and sublingual glands are involved alone, or coincidently. Recovery confers immunity.

Epidemic parotitis is a catarrhal inflammation of the duct and its branches which contain in their lumena desquamated epithelium and round cells, accompanied by hyperemia and serous and cellular infiltration of the interstitial and interglandular tissue as well as the cellular tissue bordering the parotid. The lobe of the ear is lifted. Usually the swelling subsides to normal; very rarely it leads to suppuration or gangrene, or to chronic thickening and induration.

The complication of swelling of the testes is interesting; this parotid orchitis, usually unilateral, occasionally only of the epididymis (Eichhorst), occurs especially in young adults, more rarely in children, but other organs are sometimes involved, such as the breasts, ovaries (Ruge), and the external female genitalia, occasionally the pancreas also, which may be followed by glycosuria, lipuria, fatty diarrhea, etc., (Neurath, lit., Cheinisse). Conversely parotitis has been observed after ovariotomy (and laparotomy) (v. Preuschen, R. Levy). The testicle usually reveals a slight hydrocele; atrophy is relatively rare, but Hall (lit.) found a delicate fibrosis. Dopter (lit.) emphasizes the meningitis of mumps, said to occur in 10% of cases and characterized by sudden appearance and usually favorable course with lymphocytes in the cerebrospinal fluid.

(2) Secondary parotitis (phlegmonous parotitis), uni- or bilateral, onset sudden, may be caused by continuity of an inflammation in the mouth or a neighboring organ (lymph node, maxillary articulation, etc.), by infectious diseases, such as typhoid fever, scarlet fever, diphtheria, etc., or in conjunction with any other active inflammation, *e.g.*, a purulent carcinoma of the uterus. The pyogenic organisms concerned, usually staphylococci and streptococci, ascend from the oral cavity (Hanau) or reach the parotid via the blood stream as emboli. The former seems more frequent; at least, microscopic findings show micrococci and pus chiefly within and in the vicinity of the gland ducts.

But Rost demonstrated experimentally what R. Levy pointed out, viz., that in hematogenous infections of the parotid there is always primarily an inflammation of the ducts with excretion of bacteria and without the presence of an embolic focus in the blood vessels. It is therefore impossible to decide from the anatomy whether parotitis is ascending or hematogenous in origin.

When pus collects within the acini, the gland epithelium becomes granular, cloudy, and undergoes fatty degeneration. Thus, small abscesses are formed which may coalesce and enlarge. The interstitial tissue often becomes phlegmonous, infiltrated by serum, fibrin, cells, small hemorrhages and abscesses. Occasionally there is sequestration and suppuration of parts of the parenchyma. The gland is enlarged, its section surface extremely mottled, and a cloudy, thick or puriform fluid escapes; the lobules are large, some red or black red, others yellow, gray yellow and opaque, the interstitial strands are broad and moist. Here and there are pus foci from which green yellow droplets may be squeezed out. As the inflammation extends to the vicinity, which is the rule, the whole region becomes enormously thickened, infiltrated and as hard as a board.

(For surgical diseases of the salivary glands, see Kuttner, "Textbook of Practical Surgery," 1913, and Heineke, "Injuries and Surg. Diseases of

Salivary Glands," Stuttgart, 1913; Honigmann, "Independent Acute Purulent Inflammation of Salivary Glands," D. Z. Surg., 160, 1920.)

The skin, usually anteriorly, is often perforated like a sieve. Occasionally the inflammation extends along the facial nerve which may remain paralyzed after the process subsides, or spreading still further, it penetrates the middle ear (deafness), or along the trigeminal to the skull cavity. Sometimes abscesses are followed by phlebitis, progressing to the jugular and the sinuses in the base of the skull, especially the cavernous sinus.

Abscesses healing by scar tissue may result in stenosis of ducts.

Chronic inflammation of the salivary glands may lead to partial atrophy of the parenchyma, lobulation and connective tissue induration. The latter is said to be a starting point of tumors (sarcomas, enchondromas) (?).

A chronic inflammation of unknown genesis consisting of granulation tissue rich in plasma cells with a tendency to connective tissue formation leads to destruction of the parenchyma and to the so-called inflammatory tumors, not attached to the skin, indolent, in the depths, fairly fixed, occurring at any age (submaxillary and parotid); they are easily mistaken for true tumors (Kuttner, v. Reuss and histological details by Steinhaus, Thaysen, Ferrarini). Soderlund points out that some are due to a masked actinomycosis. In lead poisoning (p. 550), the parotid and submaxillary glands may become firmer and nodular in consequence of pericanalicular connective tissue sclerosis (lit. by Cornil-Ranvier). (Compare the analogous inflammatory tumors of the pancreas, especially the head.)

**Ludwig's Angina or Cyanche, (dog collar),** is a very acute phlegmon of the upper lateral regions of the neck and the floor of the mouth, characterized by fever, sepsis and possibly fatal edema of the glottis, sometimes appearing in epidemics. It starts from the submaxillary gland, but according to v. Thaden, from an acute bubo of the lymph nodes below the maxillary angle, and at once invades the vicinity. It shows a tendency to abscess formation and liquefaction, and may spread from the cellular tissue below the chin to that of the anterior surface of the neck. It also extends to the deep tissues of the neck, and eventually to the mediastinum and pericardium.

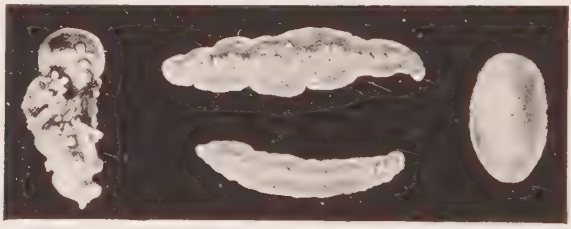
**Infectious Granulation Tumors.**—Tuberculosis may appear in the form of miliary nodules in general miliary tuberculosis. A localized chronic tuberculous parotitis is very rare (v. Stubenrauch, Bockhorn, Scheib, Puppel, Klotz, Homuth, lit.), and may, as the author saw in a 48 year old woman, be clinically mistaken for a true tumor. Tuberculosis is usually diffuse; the organ is irregularly filled with caseous nodules and miliary abscesses, or shows a chronic interstitial granulating inflammation (Kirch), or circumscribed cold abscesses or cystic cavities with flabby walls containing tubercles. Lymph nodes sometimes contain inclusions of

parotid lobules (Neisse), and the lymph nodes themselves may become tuberculous. According to Konig, a lymph node situated within the parotid becomes tuberculous as in a case with symmetrical tuberculous lymphomas the size of a walnut, diagnosed symmetrical congenital tumors of the parotids. See Kirch (lit.) for details of tuberculosis of the salivary glands.

Syphilis may appear in the form of gummas resulting in disintegration of tissue or cicatricial changes (very rare, see Letulle and Vuillet). Faroy describes congenital syphilis with the discovery of spirochetae.

Actinomycosis may cause a board-like swelling with later softening (W. Muller, Bruning, Hosemann, Guttmann, Chiari); it is secondary or primary (ductogenous); the latter, according to Soderlund's (lit.) investigations, is not rare (Schwarz).

**Salivary Calculi. Occlusion of Ducts. Salivary Fistulae.**—Foreign bodies may become lodged in the ducts of the salivary glands, and become




FIGS. 261–264.—Calculi from pancreas and salivary glands; a, from pancreatic duct; b, (above), from sublingual duct (Bartholin's); c, from Wharton's duct (submaxill. gland); d, from Stenson's duct (parotid gland); nat. size.

the nuclei of concretions; other calculi in the ducts, less frequently in the gland lobules, are produced by precipitation in thickened secretions of calcium carbonate and phosphate and a laminated organic substance which may consist for the most part of bacteria. Salivary calculi, sialoliths, are elongated, cylindrical, rosary-like, pointed or coralline; others (intra-glandular) are ovoid, usually small, but may reach a length of several centimetres and the thickness of a thumb.

The author saw a calculus composed mostly of calcium carbonate which weighed dry 9.5 gms.; it was 3.1 cm. long, 2.5 cm. broad, and one end showed a hemispherical convexity; the other was somewhat bevelled. It had been removed from Bartholin's duct of a man (collect. Gottingen).

Permanent obstruction to the discharge of saliva, *e.g.*, from a salivary concretion or cicatrix of the duct, produces salivary swelling, a sialocele (comp. ranula, p. 574). But the presence of a stone may also initiate inflammation of the excretory duct, which continues into the gland tissue, leads to atrophy of the parenchyma and connective tissue induration.

Dilatation of the ducts of the parotid by air, etc., into bulging sacks (pneumatocele) occurs in glass blowers (Narath), in musicians using wind instruments, who blow from their cheeks instead of abdomen, etc. Dorendorf saw it occur in a bugler, the author in a bag pipe player.

Salivary fistulae are recognized as external, when they empty through the skin, and internal, when they empty into the mouth cavity. They may be duct fistulae or gland fistulae, and are due to trauma or ulcerative processes.

**Tumors of the Salivary Glands and Parotid Region.**—We must differentiate between tumors which demonstrably arise from the salivary glands, first from the parotid and then the submaxillary, and those which develop in the parotid region from misplaced parotid gland rests, (Guleke), always remembering that some tumors truly derived from the parotid are soon lifted above the level of the gland and remain merely in loose connection with it.

According to Weishaupt (lit.), in considering the origin of cysts and tumors in the vicinity of the lateral angle of the mouth cavity, around the reduplication fold of the upper mucosa of the cheek on the lower, the embryonal lateral tract, the mandibular branch of the parotid duct, must be remembered as a solid epithelial body supplied with crypts.

**Epithelial Tumors.**—Among epithelial tumors, there are: (*a*) the benign, rare, pure adenomas, but slightly movable, of slow growth, soft consist-

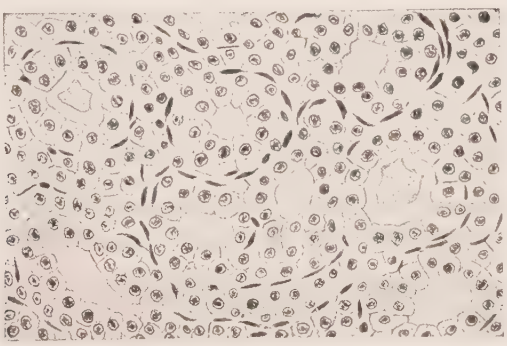


FIG. 265.—Adenoma of parotid; a soft tumor the size of an almond; woman 42; (high power).

ency, nodular and lobulated, of simple glandular structure, sometimes small, sometimes large cystic and the hard adenochondromas. [See Schutz, C. B., Am. J. Path., 2: 153: 1926.—*Translator.*]

The author has seen papillary cystadenomas, and cystadenomatous development with wide gland spaces in a thick-walled cyst.

(*b*) The malignant epithelial tumors appear as soft adenocarcinomas of rapid growth, or, the rarer scirrhous carcinomas, or squamous cell carcinomas, in which giant cells may appear among the polymorphous cells,

as the author saw in a 71 year old man. These are usually met in more advanced age. Some forms grow slowly, others grow rapidly, the softer the tumor, the more rapid the growth. They quickly invade adjacent tissues, and soon cease to be movable in relation to their surroundings.

In contradistinction to these are the benign tumors especially of the parotid, among which the so-called mixed tumors are the most frequent (p. 600). They are nodular, firm, grow very slowly, encapsulated, mov-

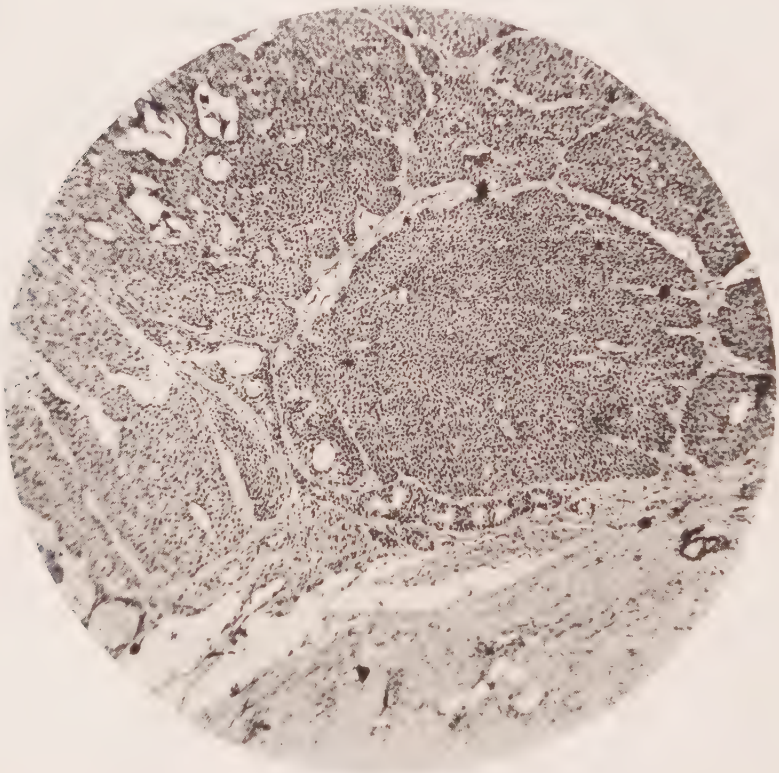


FIG. 266.—Adenoma of the salivary gland (published by C. Shutz in Am. J. Path., 2:153:1926). × 120. L. H. #19166.

able in reference to their surroundings, and during extirpation, almost pop out.

Carcinoma may also develop by malignant change in a typical benign mixed tumor, again a proof of the epithelial nature of these much discussed growths. The tumor often remains stationary for years, then grows rapidly to considerable size, infiltrates its vicinity, ceases to be movable, penetrates the skin, recurs, and produces metastases.

The author saw a papillary cyst carcinoma the size of two fists in a 58 year old woman, said to have developed in one year, which perforated

the skin like a fungus. Besides the characteristic pictures of papillary cyst carcinoma, the tumor showed resemblances to the cylindromatous structures of the so-called mixed tumor in the form of hyalin masses within epithelial plugs, or in the gland lumena (p. 600); the hyalin degeneration and granular disintegration of the epithelium were similar to that in adamantinoma (p. 590); in other parts there were metamorphoses into pavement epithelium with pearly arrangements.

**Connective Tissue Tumors.**—Among tumors of the connective substance group, especially in the parotid, the fibromas are rare, chondromas more frequent, and all forms of cartilaginous tissue are met. Chondromas are almost always benign, rarely exceed the size of a hen's egg, are hard, nodular and hyalin on section, often partly myxomatous or fibrous, lobulated and not rarely cystic. The cysts contain a mucinous water-clear, or a sanguinous brown, cloudy or clear fluid; calcification and ossification are present at times.

Pure chondromas, thought to originate from the branchial arches, or misplaced primitive ear cartilage, are rare; usually, cartilage is a part of a so-called mixed tumor, which may, at times, appear like a pure chondroma because of recession of other tissues.

Lipomas usually originate in the vicinity of the salivary glands. Hemangiomas, sometimes voluminous and of quick growth, belong to the hyperplastic capillary hemangiomas. They develop in the parotid region displacing the glandular elements or possibly prevent their development and allow only ducts to remain preserved. These portions of the parotid become changed into a granulo-acinar gray red tissue, in which vessels are not always visible macroscopically, while in other cases, they are spongy and vascular; the other parts, usually peripheral, remain free.

The skin over the tumor is stretched, thinned, dark red, and may be invaded. Hemangiomas are considered rare, occur in young children and some are congenital. In addition to the two cases reported by Usui (lit., with histologic pictures), the author saw 4 more in female children: age 4 months, tumor observed at birth, then the size of a fist; age 6 months, the size of a chestnut, had invaded the skin; age 1½ years, the size of a fist; 1¾ years, exceeded the size of two fists (Herxheimer, lit., and Hagetorn, whose specimens the author checked, also Ittmann, v. Haberer, Harras and Suchier).

Lymphangiomas are quite rare, but may occur symmetrically in both parotids (E. Hagenbach). See p. 284, also Ferrarini for peculiar so-called "branchiogenic papillary cyst-adeno-lymphomas" of the parotid region.

Sarcomas are relatively rare; there occur spindle cell, fascicular, round cell (very rare; Schridde, lit.), polymorphous, large cell (the author saw one in a five year old girl), and pigmented types. The latter, called by

some "melanomas," may have both very large angular and spindle cells, as the author saw in a man 36 years of age. They may remain well encapsulated for a long time, shell out easily and offer a good prognosis, or be very malignant tumors, quickly growing, infiltrating and finally perforating the skin; regional metastases, however, are quite rare in spite of this.

Sometimes there is a clear relationship between the sarcoma cells and blood vessels, the cells forming a collar around the vessels (perivascular sarcoma, a form of angiosarcoma). The cellular masses may thus be interwoven (plexiform angiosarcoma); sometimes hyalin changes are extensive in the vessel walls, and the blood-filled, very narrow lumen lined with endothelium is surrounded by a thick zone of hyalin tissue joined further out by sarcoma cells (angiosarcoma, or perithelioma with hyalin change of the vascular walls; see illustration under meninges; generalities in reference to angiosarcomas, p. 179, and under pia mater).

**Mixed tumors** (so-called) are benign growths, sharply outlined from their surroundings and comprising the typical neoplasm of the parotid (C. Kaufmann, Nasse, Volkmann) and the submaxillary glands (Kuttner, Chevassu). Clinically (p. 598), they are quite characteristic, but histologically show a complicated structure. The ground and interstitial tissue consists of myxomatous material or cartilage with transitions of one into the other, small amounts of hyalin or fibrous vascular connective tissue, here and there some flat, lymphoid tissue or bone. Within this basic tissue are found inclusions varying in mass and appearance in the individual cases, consisting of more or less closely packed, small, elongated to spindle cells, frequently arranged in basket works, networks, strands, branching columns, or gland-like tubes lined with cubical or cylindrical epithelium, occasionally dilated to cysts, with hyalin contents in the shape of cylinders, hence the old designation "cylindroma," (figs. 268 and 269), or irregular larger complexes (as in sarcomas). These cells are frequently lost in a fibro-mucoid mass or pass into cartilage without any sharp boundaries. Altogether the doubtul demarkation of the cellular masses and the blending of the various different tissues is very characteristic (fig. 268). Transitions of salivary gland tissue into tumor cell masses also occur. Sometimes the cells are arranged in whorls as in epithelial pearls. Thus far an agreement has not been reached as to the nature of these cells, whether endothelial, derived from the endothelium of lymph and tissue spaces, or epithelial; the latter origin has the more adherents at present.

After investigating approximately 50 specimens, the author has decided to join the supporters of the epithelial theory. The extremely variable pictures in basal cell carcinomas or basaliomas, and in the enamel organ and its tumors (figs. 257 and 258) have demonstrated the possible vari-

ability of ectodermal cell proliferation, especially the transition of ectodermal into apparently mesenchymal figures. The similarity to glands and the cylindrical cells speak for the epithelial nature of the tumors of salivary glands, but additional proof is furnished by the finding of pavement epithelium, pearls, cornified pearls, prickle cells and occasional protoplasmic fibrillation. Quite similar tumors occur on the cheeks, nose, lips, chiefly on the upper lip (one in a man of 45 years, tumor size of a plum,

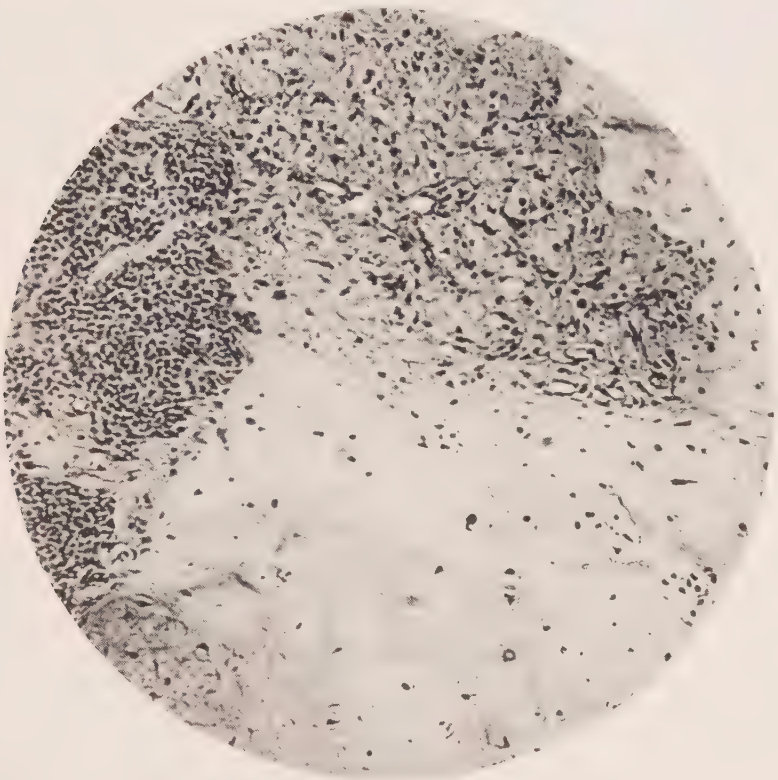


FIG. 267.—Mixed tumor of the parotid showing cartilage, epithelial cells, lymphocytes and connective tissue. In the translator's experience, the most characteristic content of mixed tumors of the parotid is cartilage. Such pictures as this cannot always be found on first examination. A number of sections may be necessary to reveal its presence. An important deduction from this is that no parotid tumor should be regarded as anything other than a mixed tumor until satisfactory evidence of the absence of cartilage has been procured, i.e., the mixed tumors of the parotid are so much more frequent than others that they must be excluded before a positive diagnosis of another tumor is made, especially so because some contain large amounts of epithelium and relatively little connective tissue while others contain the opposite. (See McFarland, J., Am. J. Med. Sci. 172:804:1926.) × 120. L. H. #19928.

existed for 20 years), gums and, as in a 15 year old girl, also in the lobe of the ear. (Lit. by Semjonoff and Lenormontd-Duval-Cottard, Krompecher, Guleke, Bruggemann.) The ectodermal tumor cells show their capacity to assume the appearance of mesenchymal tissue by forming fibres and interstitial substance; they may develop a "pseudostroma"

imitating connective tissue (Krompecher). These sarcoma-like pictures in "mixed tumors" of the salivary glands, with their close juxtaposition of spindle shaped epithelial cells, their plexiform cell strands and fibrillar formation have their analogy in other well known ectodermal tumors; it might be pointed out that the epithelial cells of the neuroglia have the faculty of changing into a fibre network. In reference to the "cartilage," Marchand believes it probable that it also originates from epithelium, thus the name "pseudo-cartilage," *i.e.*, areas in which epithelial cell strands separate into single cells which become enclosed in a homogeneous ground substance.

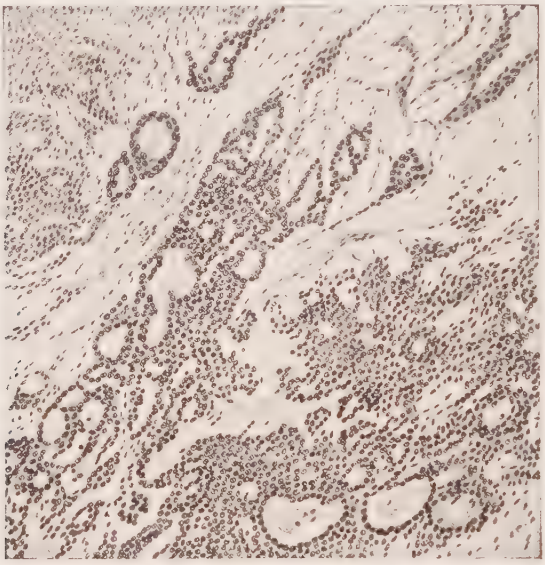


FIG. 268.—Benign so-called mixed tumor of the parotid. Epithelial cells, some in glandular form (with hyalin cylindrically shaped contents) some in heaps show transition into strands and reticulum which often gradually become lost in fibro-mucoid tissue; woman 51, (med. magn.).

Bottner, following Ehrich, considers the mucous as well as the cartilaginous tissue a metamorphosed product of the secretions of these tumors which he calls "secreting epitheliomas of the salivary glands." Bottner is probably correct when he assigns a very unimportant part to the mesodermal elements (mesenchyme-connective-tissue-blasts), meaning the connective tissue with vessels in these tumors. Those tumors, even of long duration, which consist chiefly of mucus, and still more frequently of cartilage, and for which the conception of a scattered anlage or a mesodermal origin is very tempting, are, according to Bottner, merely tumors in which there was recession of the plainly epithelial structures. Bottner does not like the term "mixed tumors" since they are in reality uniform benign epithelial neoplasms.

Besides the authors named, Hinsberg, Ribbert and Chevassu pointed out the epithelial origin of the cell formations under discussion, and Fick, Krompecher, Marchand and Ribbert emphasize them especially. Wilms believes they are derived from scattered germinal tissue (epithelial and connective) of the oral invagination; undoubtedly the simplest explanation is to assume a relationship with embryonal disturbances, such as displacement of ectodermal cells at the time the salivary glands and gill arches are formed (cf. Hinsberg, Wood, Chevassu, etc.). While most investigators do not doubt there is a congenital anlage behind these tumors (Harbit, etc.), Bottner, and Ehrich assume they start, as a rule, in the finished

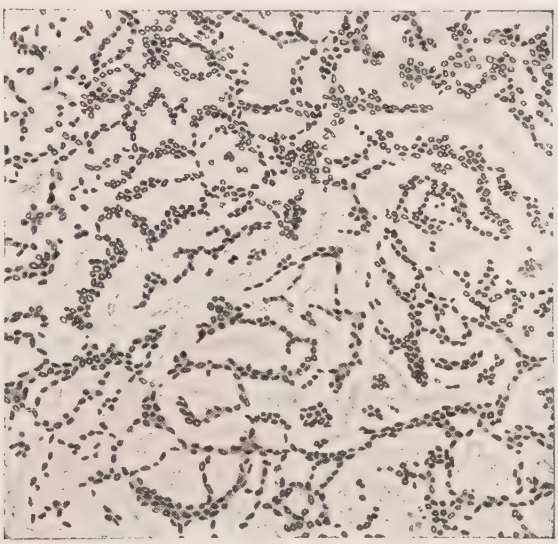


FIG. 269.—Benign so-called mixed tumor of the parotid; epithelial cell cords fringing out in delicate twigs, lying and being lost in a fibro-mucoid tissue; girl 21 years old. In other places the structure was like that in fig. 245. (Medium magn.).

gland, even several decades after birth. Volkman defends the idea of endothelial origin (Institute Marchand), also Steinhaus, Martini, Hansemann; Borst also has not quite abandoned the endothelial theory. The author saw a few cases in which the presence of cystic lymph containing (?) spaces, lined with flat cells as in well known lymphangiomas, showed that an endothelial derivation is possible exceptionally (lit. in appendix).

Microscopically, the inexperienced may mistake them for sarcomas or carcinomas, but the macroscopical examination showing a closed, encapsulated tumor should protect them. This capsule is also a clinical demonstration of its benign character, always remembering, however, that cases of malignant metamorphosis do occur (pp. 598 and 599). [See McFarland, J., Am. J. Med. Sci., 172: 804: 1926.—*Translator.*]

Symmetrical simple lymphomas are rare (p. 264), but the interstitial tissue of the salivary glands does contain abundant lymphoid tissue (Rawitz, Ferrarini, lit.). These (probably infectious) symmetrical regional lymphomas have been simultaneously observed in the lacrymal glands, salivary glands and the pharyngeal wall (Mikulicz, Fuchs, etc.), and called a "peculiar symmetrical swelling of lacrymal and oral salivary glands," or Mikulicz's disease. Mikulicz describes the tissue as consisting of small round cells, Fuchs speaks of lymphomas, Tietze of lymphoid tissue, or adenoid proliferation, Kummel, Kuttner, of lymphocyte infiltration. Kulbs found diffuse or focal lymphocytic infiltration, epithelial degeneration, giant cell formation and considerable connective tissue, and he speaks of a chronic inflammatory process. The cases of Zirm, Axenfeld and Haeckel show that exceptional transitions occur between this regional, simple lymphoma formation, which might be called aleucemic (Orth) and aleucemic adenia, and Hochenegg emphasized that the eventual enlargement of lymph nodes and of the spleen in Mikulicz's disease approximates it still more closely to the pseudoleucemic symptom complex. Reiche also declares this disease is a symptom of a general condition, lymphomatosis with swelling of the spleen and a typical blood picture. Besides the pure isolated form (Mikulicz), others show symptoms of constitutional lymphatism, or of swelling of lymph nodes without blood changes, *i.e.*, pseudoleucemias (Thaysen) or lymphogranulomatosis (Hodgkin's disease) (Gaisbock). These conditions have little in common with the strict conception of Mikulicz's disease; especially is this true of leucemic lymphomatoses of lacrymal and salivary glands (Gallasch, Delens). (Lit. in appendix.)

Care is necessary in the differential diagnosis not to mistake these for chronic tuberculous hyperplasia of lymph nodes (pp. 259 and 596) or for symmetrical lymphangiomas of the salivary gland which are very rare.

## PALATE, TONSILS, PHARYNX

The mucosa of the palate and pharynx is rich in lymphatic tissue in diffuse infiltrations and circumscribed nodules; white blood cells wander to the surface (see below). The non-cornifying epithelium of several layers covering the palate and pharynx (in the upper part there is also some ciliated epithelium in layers) dips from the surfaces of the two palatine tonsils and the single pharyngeal tonsil into many crypts and lacunae in the loose lymphatic structure of the tonsils. The palatine tonsils are lympho-epithelial organs; solid epithelial buds develop spaces by loosening of the cells into a reticulum into which lymphocytes wander. Numerous lymph follicles near the surface, the crypts (fig. 270) and the adenoid

tissue of the lingual follicular glands allow lymphocytes and occasionally leucocytes, the latter in the presence of inflammation, etc., to reach the crypts and the free surface (Stohr; Renn). In the buccal secretion they are the so-called salivary bodies, but see Gott, Laquer, Hammerschlag, lit. Weinberg, in reference to leucocytic forms, and the opinion that salivary bodies are leucocytes. The crypts always contain bacteria, among them streptococci (Henke and Reiter) and desquamated epithelium. There are often a large number of karyokinetic figures in the tonsillar follicles. The intact mucosa, the lymphoid pharyngeal ring, but especially the tonsils, are permeable to virulent bacteria, chiefly through gaps in the epithelium (Lexer), and may be the portal of entry of a local or general infection (Citron); less virulent bacteria always present in the buccal cavity, may also enter the tissues probably through minute lesions of the mucosa, *e.g.*, in circulatory disturbances due to colds with decrease of the bactericidal substances of the tissues (comp. under pneumonia, p. 404).

### Circulatory Disturbances

Oligemia of the palate and pharynx is manifested early in general anemia and is often an early symptom of phthisis.

Hyperemia. Congestive hyperemia may be caused by the most diverse irritants of thermic, chemical and infectious nature; it is manifested by redness of the parts. Chronic hyperemia with mild brown pigmentation is often seen in smokers and drinkers.

Of practical importance is the fact that some acute infectious exanthematous diseases, such as measles, scarlet fever, German measles, etc., in the stage of incubation, before the skin eruption is present, very frequently show spotted or striated reddening (mucosa exanthem) on the palate and pharynx, which are possibly the portals of entry. In measles, see Koplik's spots, p. 549.

Passive hyperemia swells and discolors the tissues blue red, and it occurs especially in drinkers. Long continued venous hyperemia produces small phlebectasias in the mucosa.

Edema may be of inflammatory local origin, such as trauma, burns, ulcerations, tonsillar abscesses or by continuity from the vicinity, spinal column, parotid, etc. In some cases, it is purely mechanical and passive, as in tumors of the neck, such as lymphosarcomas, carcinomatous infiltration of cervical nodes, etc.

The soft palate and the uvula are especially subject to swelling, the latter appearing like an edematous polyp. Edema of the larynx may result from an inflammatory edema (p. 307).

### Inflammations

Inflammations involve all of the palatine mucosa and the tonsils, or are confined to isolated parts; the names used are angina, uvulitis, tonsillitis; angina has reference to diseases of the palate and tonsils.

Angina and pharyngitis, often combined, are idiopathic, or symptomatic.

The various general causes of disease are of etiologic importance, *i.e.*, mechanical, chemical, thermal and parasitic infections. In simple catarrhal inflammations "cold" is a factor according to age-long experience, even if only predisposing (p. 404); the infection may appear from without or within (autoinfection).

Schoneman considers the pharyngeal tonsils are subepithelial cervical lymph nodes, draining the nasal mucosa, and acute lacunar angina tonsillaris comes from nasal infection by way of the lymph channels.

**Acute Catarrhal Inflammations.**—In acute catarrhal angina and pharyngitis, the parts are spotted, striated or diffuse red; the secretion is mucoid, mucopurulent or purulent. Loss of epithelium leaves an erosion from which a flat, so-called catarrhal ulcer may develop. Vesicular exfoliation (vesicular angina) is found very early on the hard and soft palate in smallpox analogous to the vesicular eruption of the skin, and in herpes (usually labial or facial). If the vesicles rupture, there result small suppurating ulcers. In glandular angina, mucous glands with their ducts occluded become nodular.

On the tonsils, differentiation is made between a surface catarrh, tonsillar angina or superficial amygdalitis, and one in which the crypts are coinvolved, lacunar amygdalitis, or, erroneously, follicular tonsillar angina.

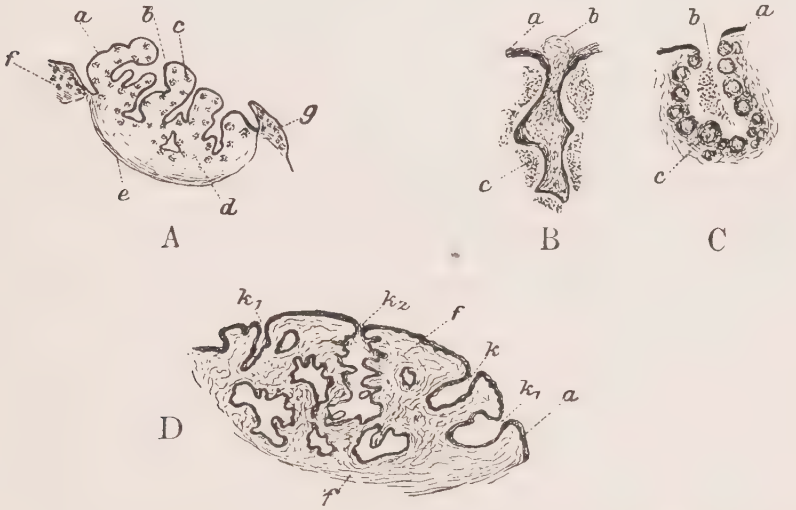
According to Maclachan, an acute inflammation of the tonsil always commences in a crypt as a defect in the epithelial covering—primary effect, analogous to the primary effect in the appendix (according to Aschoff). The proof of such a generalization is difficult.

In lacunar angina, the tonsils swell, the crypts fill with yellow or gray yellow masses of purulent appearance, consisting of mucus, desquamated epithelium, fatty debris, pus cells and bacteria. These plugs, often foul smelling, project from the lacunar openings (fig. 271) as yellow spots and may be mistaken for pus foci or abscesses. They may be squeezed out, or become confluent on the tonsillar surfaces and thus look like a pseudomembrane. But these plugs are often firmly attached and by absorption of calcium salts from the mouth fluids become tonsillar calculi (amygdaloliths), but still may consist partly of soft foul-smelling debris. Sometimes tonsillar calculi are several millimetres in diameter, occasionally they reach the size of a pea or more. They may sustain a chronic inflammation

of the crypts or cause recurrent inflammations, or in time lead to tonsillar atrophy.

According to E. Wagner, in superficial catarrhal tonsillar angina, the epithelium, even on the palate (mistaken for pseudomembranes), may be so permeated by leucocytes that delicate yellow spots and striae appear. These may be easily wiped off.

In true follicular angina, a rather rare disease occurring as well in the follicular tonsils as on the palatal mucosa, the follicles swell, become purulent and rupture, leaving small ragged ulcers. In some chronic




FIGS. 270–273.—A. diagrammatic horizontal section through left tonsil in situ; a, surface epithelium; b, crypt; c, follicle; d, loose tonsillar tissue; e, base of tonsil; f, palato-glossus muscle; g, palato-pharyngeal muscle. B. A crypt in lacunar tonsillitis; a, surface epithelium; b, crypt with plug; c, adjacent follicle (diagrammatic). C. From a chronic hypertrophic tonsil; Crypt (b) with adjacent markedly projecting follicle (c), thickening of fibrous ground substance. D. Fibrous transformation of a tonsil; atrophy of follicle; deepening and dilatation of crypts at K1, and K1, and especially at K2; f, fibrous tissue.

hypertrophies, the follicles are thickened. It is quite important to remember that catarrhal angina is one of the constant initial symptoms, even before the eruption of the exanthem in a number of the exanthematous acute infectious diseases, such as German measles, measles, (chiefly spotted redness of the posterior arches), scarlet fever (uniform reddening of palate and tonsils), etc. The mouth cavity is probably the portal of entry of the infection. Catarrhal angina is the mildest form of pharyngeal inflammation in scarlet fever; severer forms, the so-called parenchymatous angina, are very frequent, and abscesses or necrosis or gangrene may develop on the third to the fifth day as a scarlet diphtheria with necrotizing characteristics (cf. p. 613 "pharyngeal diphtheria").

Much attention is paid to the tonsils in cryptogenic infections, and lacunar angina is blamed as the starting point of many infectious processes (Bachhammer, lit.), especially articular rheumatism, but other parts of the oral cavity must also be considered (p. 604).

**Pseudomembranous Inflammations of the Palate, Tonsils and Pharynx.**—Superficial and deep membranous, pseudomembranous, croupous, diphtheritic, necrotizing or whatever they may be called, inflammations may be due to many causes such as burns, cauterization, various infectious diseases, especially scarlet fever, occasionally measles, smallpox, typhoid fever, dysentery, influenza (Verse). Specific membranous inflammation of the pharynx and the upper respiratory tract, or epidemic diphtheria, will be discussed separately on account of its great importance. (See data under membranous inflammation of the larynx, p. 311.)

True pharyngeal diphtheria, or epidemic diphtheria, or simply diphtheria, or diphtheritis, croup, contagious synanche or synanche, is an acute infectious disease appearing mostly in children, but also in adults, when it tends to be especially severe, localized to the palate, pharynx and tonsils, causing an inflammation of varying severity and pseudomembranous in characteristic cases; it often extends to the upper respiratory passages. Rarely the larynx is the primary site. The cause is the Klebs-Loeffler diphtheria bacillus.

(F. Meyer gives a good resume of the history of diphtheria.)

Diphtheria bacilli cause not merely a local pseudomembranous inflammation at their place of growth, but by poisonous substances (toxins) distributed throughout the whole body from the local focus of disease, cause severe general intoxication and organic changes, especially in the heart and kidneys. Diphtheria bacilli and the immediate changes produced by them are thus usually found only at their portal of entry and in the deeper layers of the membranes, otherwise, nowhere else in the body, and although the organisms have been found in regional lymph nodes and also in internal organs, *e.g.*, in bronchopneumonic foci, this is by no means the rule. Lately the number of observations of diphtheria bacilli in the urine, and in the lungs (macroscopically unchanged) has increased in fatal cases, while they have rarely been found in the circulating blood, the bile or in the spleen. Accordingly diphtheria, like any other infectious disease, may be accompanied by bacteremia (lit. in appendix).

Loeffler's diphtheria bacilli are non-motile rods approximately the length of a tubercle bacillus, but twice as thick, smaller in young cultures, longer in older ones and not rarely club-shaped in their bodies or ends. They grow best on coagulated blood serum (Loeffler); in 6 to 24 hours they form small gray white rounded colonies. They stain best with alkaline solution of methylene blue (Loeffler), and are Gram positive. Of practical

importance in their differentiation from similar bacilli, is differential staining with methylene blue and vesuvin, whereby the body of the bacillus stains pale brown and contains dark blue oval granules usually at both or one end, but according to M. Neisser, this appears only when the bacilli have been cultured for 9 hours at 35° C. In sections, they can be demonstrated with Gram's stain; in older cases, complicated by mixed infection, they are obscured by other organisms. Diphtheria may be transmitted to various animals, such as rabbits, chickens, pigeons, mice (which were formerly thought to be absolutely resistant, see lit. by Kolle and Schlossberger), and especially to guinea pigs, which are most sensitive; in places previously traumatized, infection can be established (trachea, vagina, conjunctiva) with a pseudomembrane; with high fever and paralysis, the animals die in a few days. Edema, inflammation of serous membranes, etc., are found; apart from the spleen, no diphtheria bacilli can be found, as a rule, in the internal organs. Therefore, the results must be due to toxins, and these prepared by Brieger and C. Frankel, etc., can be so adjusted in their dosage to kill the experimental animals in days, weeks or months. Filtered bouillon cultures, free from bacteria, kill guinea pigs in 2 to 3 days. The organisms are exceedingly resistant; Loeffler found some virulent bacilli in dry pieces of membrane as old as 14 weeks; when somewhat moist, they remain virulent for 7 months. At 50° C., they die in ½ hour. They retain their virulence in the oral and nasal cavities of convalescents for three weeks or more (Busing). The diphtheria bacilli of carriers are just as dangerous to others as those of the severely sick. Petruschky attempted to cure carriers by active immunization, *i.e.*, the subcutaneous injection of diluted vaccine of cultures from their own diphtheria bacilli. More details in relation to carriers by Schweriner. Dissemination takes place by contact infection, droplet infection (Flugge), dry dust (Germano), and probably also via the urine (see above). In some cases infection with living diphtheria bacilli causes no symptoms or only a slight angina, depending on mild virulence of the organism or good resistance of the infected individual, etc. In epidemics this is observed more frequently in adults while children suffer from severe infections. It seems that the individual predisposition of adults is slight, while small children, especially those with a "locus minoris resistentiae" such as hypertrophied tonsils have a high susceptibility, (see p. 294 in reference to the frequency of nasal diphtheria in sucklings). Lymphatic children succumb readily to the infection (Daut). Individual predisposition gradually decreases from the 6th year onward, and very quickly from the 13th year (Flugge, Grundriss der Hygiene). v. Behring's antitoxin neutralizes the specific toxins of diphtheria; it therefore is curative in pure cases, and fails in mixed infection (p. 612). For the equal curative effect of normal horse serum, see the cri-

tique of Joannovis. In the mouth and nose of a healthy person, the so-called pseudo-diphtheria bacillus may be found, and although non-pathogenic for experimental animals, it resembles true diphtheria bacilli. According to some (Hoffmann, Loeffler, M. Neisser and others), it is a separate type, while others (Roux, C. Frankel) consider them non-virulent, degenerated true diphtheria bacilli (Klinger and Schoch). According to M. Neisser, they occupy an undeservedly large place in the literature; they mean very little to the trained investigator (Scheller, Gins, Muhsam, Landau). The xerosis bacillus is almost always present on the conjunctiva (Axenfeld), and is non-virulent, but it belongs to the group of pseudo-diphtheria bacilli with a few cultural peculiarities of its own.

**Formation and Composition of the Pseudomembranes.**—The change begins as the epithelium of the mucosa undergoes partial necrosis under the influence of the infection (toxins), and is sprinkled with gray white cloudy spots. According to Heubner, very soon afterwards an exudate, at first fluid, later coagulated, rich in cells, oozes from the hyperemic, infiltrated mucosa, passes through the dying epithelium, reaches the surface, and is precipitated as a gray white or yellow white pseudomembrane. This exudation from below may be repeated in layers, the last formed lifting the superimposed strata higher; thus, the uppermost layer is the oldest, always contains numerous bacteria, but usually saprophytes, and frequently undergoes hyalin, finely granular disintegration (fig. 274). The other layers consist chiefly of a fine or coarse meshwork and dense felting of fibrin (fig. 274), enclosing leucocytes in greater or less numbers (fig. 274). Some layers consist mostly of pus cells, others of fluid; the epithelium is partly or completely destroyed under the pseudomembrane.

The heavier fibrin depends on the large number of leucocytes, and according to Weigert, appears where leucocytes predominate in the exudate. The firm fibrin is formed from the fibrinogen of the exudate and the disintegration products of leucocytes, the latter undergoing solution in the exudate and appearing like fine threads.

In the edematous, hyperemic, often hemorrhagic and cellular infiltrated mucosa, both fine and heavy fibrin is deposited; the dilated lymph and blood vessels also contain fibrin (fig. 274 in the center between bb).

Relatively rarely the mucosa itself undergoes direct necrosis to various extents (toxins). This is the true deep diphtheritic form of inflammation, and the pseudomembrane consists partly of necrotic mucosa, penetrated by fibrin; this condition usually occurs only in spots, and most frequently on the tonsils. The walls of the vessels in the mucosa undergo hyalin necrosis, and are thickened; other dead parts also undergo hyalin-fibrinoid changes (coagulation necrosis), and the glassy network containing cells, nuclear fragments and fibrin, is quite similar to the membrane. At first

the necrotic parts are fairly firm, but they soon liquefy and become detached. The necrotic areas are surrounded by small cell infiltrations (reactive inflammation). Complete healing, described on p. 313.

Picrocarmin is a very good stain (also von Gieson's stain); the fibrinous scaffolding is yellow; for more exact investigations of the fibrin, Weigert's stain is recommended; it also stains the diphtheria bacilli, which, according to Heubner, are more plentiful on the 2nd to 3rd day.

Macroscopically, the beginning of the process is recognized by small gray white spots or stipplings, usually first on the tonsils; they spread and coalesce in thick membranes plainly laminated, until they coat the

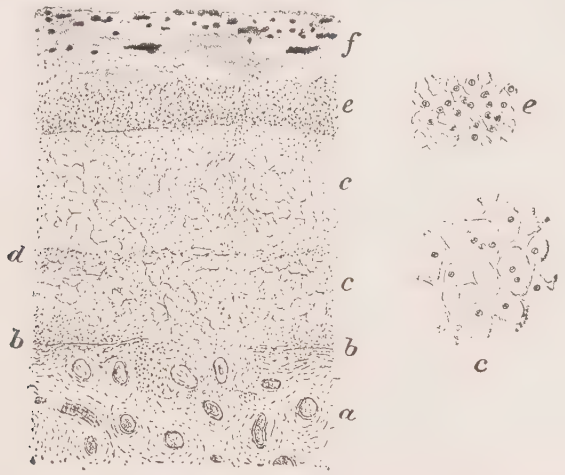



FIG. 274.—Pseudomembranous inflammation of the palate in true diphtheria. **a**, mucosa with blood vessels; b, border, where formerly epithelium was situated, membrane deposited upward. In the middle between bb the mucosa itself is penetrated by fibrin and round cells and it contains vessels with hyalin walls. c, wide-meshed fibrin network with thick fibres, but few leucocytes; d, abundant leucocytes in a closer fibrin network; e, delicate fibrin feltwork with many leucocytes; f, hyalin metamorphosis of topmost layer, contains numerous masses of organisms (black). Fig. to left, low power; e and c, high power.

pharynx, tonsils and palate, nose, larynx, trachea and even the bronchi. In the beginning, the membranes are firm and white; later they become soft and brown yellow. On areas covered with pavement epithelium, the membranes are more firmly attached (p. 312), and often white, glassy, rather hard, almost like cartilage or hardened icing, and they are much more frequently in the form of thick homogeneous plates than coherent laminated membranes; the latter are seen best in the trachea (fig. 147, p. 311).

Beginning at the laryngeal pouch, they often spread by continuity to the smaller bronchi where they are easily detachable; sometimes they are lifted off by the secretions of mucous glands and are thus spontaneously detached; in fact, detachment occurs in other places when the mucosa produces a non-coagulating fluid to lift off the coagulated coating. Under

the membrane the bright red mucosa is stippled with many minute hemorrhages. Detached membranes may be coughed up, only to form again. Sometimes the membranes are aspirated and suffocation occurs.

Membranes are usually firmly fixed to the tonsils, not merely because they are anchored into the crypts, but also because of a deep inflammatory process, truly diphtheritic in an anatomical sense (necrotizing) which also involves the vicinity of the crypts. Here develop, after detachment of necrosed portions, diphtheritic ulcers; they are most frequent in the tonsils and may become deeper and deeper by progressive necrosis.

The narrowing of the isthmus of the fauces is often marked, caused by the swelling of the tonsils and uvula; from the latter the membranes may sometimes be stripped off like the finger of a glove. After regression of the pseudomembranous inflammation the mucosa usually heals without scars, proof that the inflammation as a rule is superficial, but deep diphtheritic necroses leave scars.

**Variations in the Severity of the Disease. Mixed Infection.**—In some cases diphtheria is present only as a simple catarrh without a membrane; in other cases (mostly severe) the pseudomembranous inflammation extends to the nose, or causes laryngeal stenosis from laryngeal involvement, or is followed by croupous inflammation of the smaller bronchi, or bronchopneumonia which is very frequently fatal. But it is probable that many bronchopneumonias are not diphtheritic, but due to the aspiration of irritating substances derived from the diphtheritic parts, or to secondary bacterial invaders; it is only occasionally that nothing but diphtheria bacilli are found. It is well to remember that diphtheria bacilli may enter the blood post mortem, and be found there, while this is very rare during life (Graetz). The pseudomembranous inflammation may continue through the Eustachian tube to the middle ear, or through the nose and lacrymal ducts to the conjunctivae.

The cases showing a septic character are usually due to mixed infection with staphylococci, or more often, streptococci. They, and their toxins, enter the blood, and septic inflammation of various organs, especially the kidneys, and general intoxication are added to the diphtheria. The inflammations often have an hemorrhagic character with punctate hemorrhages in the skin, serous membranes, mucous surfaces, kidneys, renal pelves, myocardium, etc. The bronchopneumonias stand out especially and are sometimes presented in the form of innumerable blood red, firm foci. More rarely the inflammation is gangrenous; not merely the membranes are discolored, foul smelling and purulent (the latter may occur without gangrene), but the mucosa itself becomes gangrenous. Bacteria are probably always present in the oral cavity which may cause gangrene under suitable conditions (p. 550).

Plaut-Vincent's angina is an ulcerating pseudomembranous inflammation not confined to the tonsils, due to a fusiform bacillus (Plaut-Vincent bacillus) in symbiosis with spirochetae (spirochaeta dentinum, according to others, spirochaeta buccalis), much more numerous in culture than in other ulcerative processes of the mouth cavity or normally (pp. 550 and 559) when they are harmless saprophytes; furthermore, they are found in the tissues and clefts like other pathogenic organisms (lit. Rona, Babes, Bluhdorn). This disease is differentiated from pharyngeal diphtheria by its relatively severe local symptoms, such as fetid necrosis, ulceration, exfoliation of thick pseudomembranes without marked impairment of the general health, its quick appearance and disappearance, although at times it continues for months. For the differential diagnosis from primary syphilis, see Scheier; differences of the spirochaetae from spirochetae pallida and staining by Gerber. The prognosis is usually good (Reiche); severe complications, as in diphtheria, are rare (Baron). Extension of Vincent's angina to the trachea and bronchi is very rare; and even then recovery may take place (Rothwell).

**Other Changes of Organs Following True Pharyngeal Diphtheria.**—Since the disease is essentially a pure intoxication with almost exclusive local development of the bacilli, the changes in the organs are due to the toxins (exceptions, lungs, p. 611, see under endocarditis) (Graetz). Chief among them must be mentioned those in the kidneys consisting principally of purely degenerative processes of the epithelium of the tubules (Huebschmann, Fahr), clinically recognized by albuminuria. Sudden cardiac death is not rare, usually, after the conclusion of the local pharyngeal disease; for changes in the myocardium, see p. 61. Splenic tumor is usually slight (p. 232), and is often absent, more marked in septic cases; the same is true of swelling of the maxillary lymph nodes.

After the local process has run its course, other evidences of the continuation of toxemia in addition to the postdiphtheritic cardiac paralysis, are the so-called nervous sequellae, especially diphtheritic paralyses, usually observed in the first two weeks or later, and commencing in the area first attacked by the diphtheria, *i.e.*, the soft palate (nasal speech), eye muscles, vocal cords and also the muscles of the extremities. In reference to the anatomical changes—fatty and waxy degeneration—see Hochhaus, Sorrensen, Hotzen, Huebschmann.

True diphtheritic autoinfection sometimes occurs in the stomach from swallowed membranes. Digital transmission to the vulva and vagina also occurs (see under noma). There is also a true diphtheritic wound infection, as the author repeatedly observed in patients with or without diphtheria of the pharynx. Thick, skin-like, firmly attached coatings, or smeary bases, poor, bacony granulations, friable disintegrated margins, are

characteristic; there are other torpid wounds with diphtheria bacilli, but no membrane (Weinert, Nieter, Hock, etc.; opposed Wieting). The infection is probably transferred on materials such as bandages, etc.; it remains localized. Similar cases occur without diphtheria bacilli and the harmless bacillus dermophilus may easily be mistaken for the diphtheria bacillus (Rohde).

**Secondary Pseudomembranous Inflammations.**— The most important form is scarlet fever diphtheria which is the severest angina. It is a mixed infection; to the catarrhal angina produced by scarlet fever (for the "cause of scarlet fever" see Gamaleia. B. Nr. 40, 1908; and lit. by J. Koch), another infection is added, usually streptococcic. Loeffler's diphtheria bacilli are not found in scarlet fever diphtheria. The anatomic changes in the pharyngeal structures are usually much more severe than in true pharyngeal diphtheria, and clinical differences can also be pointed out. Scarlet angina, complicated by streptococcus infections shows more tendency to necrosis and gangrene than to the formation of pseudomembranes, which may be completely absent.

White or discolored spots soon deepen to necrotic scabs, gray yellow on cross section; they may exfoliate with quick, deep loss of tissue, especially on the swollen tonsils, which are frequently the only parts involved, and may be utterly destroyed.

Pure uncomplicated scarlet angina is distinguished only by swelling of the tonsils and reddening of the pharyngeal mucosa. An inflammation accompanied by loose white coatings is likewise frequent (Jochmann). It also shows little tendency to extend to the larynx, but inflammatory edema of the glottis may develop.

Swelling of the cervical lymph nodes is very marked; they are filled with fibrin and necrotic foci (Buloch-Schmorl), and may suppurate or undergo necrosis along with the cellular tissue of the neck. Fatal erosion of vessels has been observed. While the pharyngeal and the glandular involvement are about equal in true pharyngeal diphtheria, in scarlet diphtheria the glandular swelling is much more severe. Acute retropharyngeal bubo is rare, and usually found at autopsy (p. 616).

In scarlet angina the nervous sequellae are absent.

Renal involvement is much more frequent in scarlet diphtheria, chiefly of the glomeruli. Albuminuria develops at once, or, more frequently at the end of the 2nd or 3rd week of the disease, or with later nephritis of varying severity, which may cause death sooner or later, sometimes after many years (see under kidneys). See p. 627 for necroses of the esophagus.

Otitis media is also very important and occurs quite frequently (Burckhardt-Merian).

**Phlegmonous Inflammation and Abscess Formation.**—Phlegmons of the palate and pharynx are inflammatory edematous and suppurative infiltrations of the tissues of the mucosa and submucosa. They are classified according to location, as:

(1) Phlegmonous angina, caused by the common pyogenic organisms, especially streptococci, and anaerobes (p. 559), is a suppurative infiltration of the soft palate, the tonsils (and the larynx). It is usually an abscess forming peritonsillitis, extending from the tonsil to the capsule and spreading chiefly laterally and upward. But the starting point in the tonsil (a crypt, see p. 606) recedes into the background when the whole picture is developed. It may develop primarily from thermic and chemical activity, *e.g.*, after the use of the cautery iron, drinking of hot liquids, acids or alkalies. Phlegmonous angina may be secondary to scarlet angina, carcinomatous, syphilitic, and glanders ulceration.

The palatine arches and the uvula, especially, may swell enormously, become yellow and almost transparent. Sometimes the phlegmonous parts become necrotic and ulcerate. The larynx and the retropharyngeal tissues are endangered (laryngeal edema); trismus occurs and swelling of the lymph nodes of the maxillary angles is constant; usually there is high fever, but not always.

(2) Phlegmonous tonsillitis may accompany a phlegmonous or diphtheritic angina, but may also develop from a simple lacunar tonsillitis. Although sharp separation of the forms (1) and (2) appears somewhat artificial (see Aschoff), it cannot be dispensed with even if only for clinical reasons, and the pathologic anatomist aims, if possible, a potiori, to select a name. The designations "simple angina" and "phlegmonous angina" strikingly characterize the types of respective cases. The tonsils swell enormously from serocellular infiltration, diffuse or localized in abscesses in the tonsillar substance; the abscesses are frequently first localized in the follicles. They may be multiple or become confluent and sometimes completely destroy the tonsil by the necrosis.

These abscesses usually rupture towards the surface. The amygdalitis readily becomes a phlegmonous periamygdalitis, extending to the retropharyngeal tissue; such abscesses may perforate into the pharynx, and by aspiration of pus, lead to aspiration pneumonia. Mediastinitis, pleuritis, edema of the larynx, thrombophlebitis of smaller branches or even the jugular are further complications usually ending in pyemia. The author has seen cases beginning with catarrhal angina, progressing to a small abscess in the depth of the tonsil and thus escaping recognition, and ending in a pyemia. As the author, among many others, has long pointed out (p. 606), many so-called cryptogenic pyemias and other etiologically obscure suppurations must have the tonsils and their bases

excluded as starting points. Fatal hemorrhage is rare from erosion of the internal or external carotids.

(3) Gangrenous or phagadenic angina begins as a phlegmonous inflammation, or as primary gangrene in swollen discolored areas which break down into ulcers. The mucosa of the palate, all of the tonsils, pharyngeal mucosa, surface of the tongue and gums become a smeary, foul smelling mass which floats on water. Ulcers on the tongue, especially on the lateral edges, may be remarkably deep; the regional lymph nodes

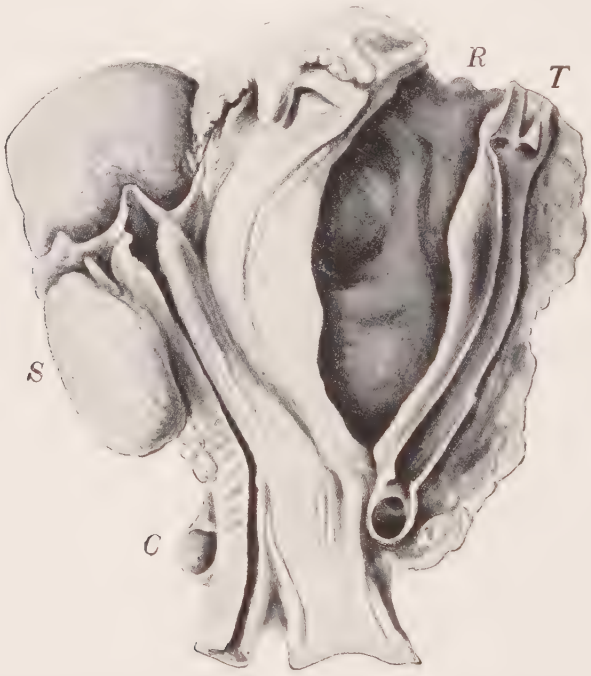



FIG. 275.—Retropharyngeal abscess, R; 7 cm. long, also partly retroesophageal; developed after angina; child 10 months old; C, 1. common carotid; T, its bifurcation into external and internal; S, left lobe of thyroid; nat. size.

are infiltrated and soften and suppurate. The condition is a sequel to true phlegmonous angina (p. 615), scarlet diphtheria (p. 614), weakening infectious diseases, chiefly typhoid fever, if the course is protracted (the author has seen maxillary necrosis), smallpox, dysentery, diabetes, scurvy, etc. Edema of the glottis or sepsis may prove fatal, but recovery does occur. The microorganisms mentioned under ulcerative stomatitis are present (p. 550).

Plaut Vincent's ulcerative pseudomembranous angina holds a relatively benign special place (p. 613).

(4) Retropharyngeal abscesses occur in connection with pharyngitis and tonsillitis, but even more frequently with various other processes

permitting access of pyogenic organisms into the loose retropharyngeal connective tissue. When a larger quantity of pus collects in the retrovisceral space between the pharynx and the cervical spine, the posterior pharyngeal wall bulges forward as a typical retropharyngeal abscess, but it may point as low as the esophageal region (fig. 275) (rare). Infancy and early childhood are preferred.

The more usual primary foci of retropharyngeal abscesses are: suppurating lymph nodes (1) in the space between the pharyngeal musculature (sup. constrictor) and the fascia of the prevertebral musculature, when the lateral pharyngeal lymph nodes (Most) suppurate secondary to a nasopharyngeal or pharyngeal infection, such as scarlet fever, diphtheria, typhoid fever. These retropharyngeal abscesses were formerly called idiopathic, and some may be due to the passage of bacteria through intact mucosa (Lexer); (2) caries of the upper cervical vertebrae or the base of the skull, usually of tuberculous origin, more rarely, actinomycotic, neoplastic or traumatic (fracture); (3) in otitis media (Kien), the retropharyngeal abscess follows perforation of the floor of the antrum or the anterior wall of the auditory canal or the tympanic cavity, or indirectly when pus in the middle or posterior fossae of the skull passes downward through the foramen ovale, rotundum or jugulare. But, according to Most, the inner ear probably also drains into the pharyngeal nodes; (4) trauma due to foreign bodies, such as fish bones, bone splinters, etc., burns or corrosions (rare). Consequences: they may be larger than a hen's egg and are impediments to respiration and deglutition; they occasionally compress the respiratory channels or rupture into them, may give rise to acute laryngeal edema, or progress downward, resulting in mediastinitis, pleuritis, etc., (Beitzke, Bartels, in reference to the lymph channels). Sometimes blood vessels are eroded. In other cases they rupture spontaneously through the posterior pharyngeal wall.

**Chronic Inflammations.**—In chronic catarrhs of the palate, tonsils and pharynx, two opposed changes may be met: hypertrophy and atrophy.

Chronic catarrh is encountered most frequently in the palate and pharynx of drinkers, excessive smokers and individuals who are obliged to speak loudly in dusty and cold air (angina cantatorum). In hypertrophic catarrh, the reddened mucosa bulges longitudinally, especially on the posterior pharyngeal wall (hyperplastic pharyngitis), or small nodules give the mucosa a granular appearance (granular angina and pharyngitis). These nodules and ridges are swellings of the follicles or mucous glands, from increase of adenoid tissue and infiltrations of the mucosa. In some areas regular tumor-like elevations are disclosed, the so-called adenoid vegetations. In atrophic catarrh (atrophic pharyngitis and angina) the mucosa is thin and smooth from fibrous changes, the follicles and mucous

glands undergo atrophy, secretion becomes scanty and dries into evil-smelling crusts. Distended veins are noticed on the surface of the thin mucosa. Focally, the mucous glands are distended by retained secretions into small cysts. An atrophic rhinitis is often coexistent.

Chronic tonsillitis, chronic tonsillar angina and pharyngitis also lead to hypertrophy with occasional acute exacerbations, or to atrophy of the tonsils.

In the hypertrophy of palatine tonsils (chronic parenchymatous amygdalitis) most frequent in children, all the parts enlarge, especially the lymphoid tissue; the follicles appear as good sized gray nodules, sometimes with yellow centers (fig. 272, p. 607). They bulge from their niches enough to narrow the isthmus of the fauces; they are firm or soft, pale, gray white or gray red. The crypts appear as narrow clefts; the deep hollow or cystic crypts of adults on the surface or within the depths of the tonsils are lacking. Chronic tonsillar hypertrophy develops in consequence of repeated acute inflammations or apparently spontaneously, *e.g.*, in scrofulous children, or in lymphatism (p. 260).

In tonsillar atrophy, *i.e.*, fibrous degeneration, the lymphoid tissue disappears and the ground tissue increases in fibrous tissue. The palatine tonsils may be of normal size when previously hypertrophic, or even be large, but eventually their size is reduced. The crypts on cross section (fig. 273, p. 607) are very deep and the organs seem to consist of individual isolated buds, while in their depths small cystic spaces are filled with bacteria and debris, or calculi. The papillae of the mucosa are hypertrophic, the blood vessel walls are thickened. This alteration in adults is due to repeated anginas. Atrophic tonsils no longer project, but are rather small hard plaques in which foci of flat or notched cartilage or bone are frequently observed in the connective tissue. These tissues are supposed to be rudiments of the second branchial arch (Orth, Deichert, etc.), as well as metaplastic connective tissue (congenital tendency, Nosske, remains of former inflammation, Schweitzer); Lubarsch mentions scar tissue encapsulating caseous calcified foci of tuberculous origin. Both origins must be accepted. (Lit. Appendix.) Such tonsils are recognizable only by occasional crypt orifices.

Senile atrophy is simple and smooth due to loss of lymph nodules and atrophy of crypts.

The chronically enlarged pharyngeal tonsil may bulge hemispherically and fill the naso-pharyngeal space, or appear as an adenoid vegetation in combed parallel rolls, running from without inward, and especially prominent in children because of much lymphoid tissue. They are softer and flabbier, while in older individuals the lymphoid tissue recedes and connective tissue predominates in the firm organs (Retterer and Lelievre,

in reference to structure and histogenesis.) They often perpetuate chronic nasal and pharyngeal catarrhs (retronasal catarrhs) and may occlude the posterior nasal orifices and tubes, the latter condition causing partial deafness. Practically, it is important to remember that adenoid vegetations are not congenital (Erdely; Czerney); some hyperplasias are due to latent tuberculosis of the pharyngeal tonsil (p. 619). A similar condition occurs in the lymphoid apparatus of the tongue from the circumvallate papillae to the epiglottis, the so-called lingual tonsil or lingual follicles.

Lacunar hyperkeratosis is the name given by Siebenmann to rare epithelial thickening and cornification until actual thorns from 1 mm. to 15 mm. long or spherical granules, are formed. Usually it occurs in younger women; the etiology is obscure, but probably not parasitic (lit. by Januszkiewicz, Milian, Urbantschitsch).

### Infectious Granulomas

**Tuberculosis.**—Subepithelial tubercles in the palatal and pharyngeal mucosa break down into ulcers more or less deep and similar to those discussed under mouth cavity (p. 554).

Tuberculosis of the tonsils, especially of the palatal tonsils, occurs as a primary infection (from food and air), or secondary, especially to ulcerative tuberculosis of the lungs. But the lingual follicles and other parts of the pharyngeal adenoid apparatus (Simon) are very apt to become involved.

H. Cramer quite lately found that tonsillar tuberculosis is secondary in 84.7%, and primary in 12.5% of cases.

Two forms may be differentiated:

(1) In the more acute younger stages, numerous disseminated tubercles are found below the surface epithelium or deep in the parenchyma. The superficial tubercles disintegrate into small ulcers with caseous bases. These tubercles are first localized in the follicles, and frequently recognizable only by the microscope.

(2) In chronic tonsillar tuberculosis the granulations are diffuse or nodular everywhere within the parenchyma, rich in giant cells and with a tendency to caseation. The cheesy masses soften, disintegrate into very deep ulcers, surrounded by tuberculous tissue. Crypts are dilated, filled with cheesy material, and surrounded by tuberculous granulations which undergo the same caseous disintegration; they become gaping ulcerating cavities emptying on the surface (fig. 276). Sometimes the tonsillar tissue is reduced to small lumpy remains. The tissue adjacent to the tonsils may become infected (musculature), spreading the process to the palate and pharynx (fig. 276), cheeks and tongue. Data vary as to the frequency

of latent tuberculosis of the pharyngeal tonsils; some consider it frequent (Pluder and Fischer in 16%), others (Piffl, Nobecourt and Tixier, H. Cramer, etc.) think it is rare (lit. by Pertik).

For the important relationship of tuberculosis of the cervical lymph nodes to tonsillar tuberculosis in children, see p. 258, and Mitchell. Primary tonsillar tuberculosis of adults is relatively benign, and probably without much importance in tuberculous infections of the lung (Bandelier, lit. by Maclachan).

Lupus occurs in conjunction with facial lupus, and may leave deep scars and deformities resembling syphilis, but more uniformly distributed (Birsch-Hirschfeld).

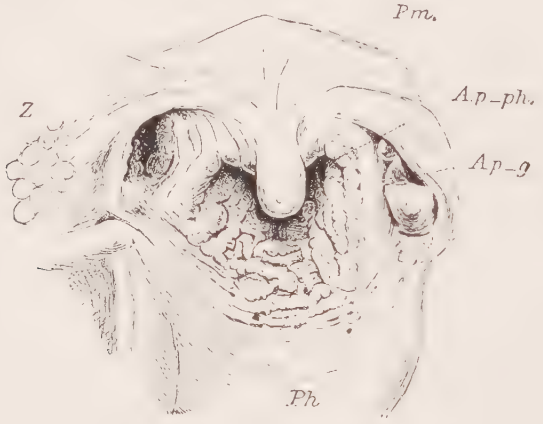



FIG. 276.—Very marked tuberculous ulceration of palate, tonsils and posterior pharyngeal wall. Ph, pharynx; A.p-ph, palato-pharyngeal arch; A.p-g, palato-glossal arch; Pm, soft palate, uvula attached; Z, tongue with follicular glands.

**Syphilis.**—The essentials were mentioned under oral cavity (p. 556), and it was stated that primary lesions may occur on the tonsils (even bilateral).

They appear as papules or scleroses; if ulcerated, as chancres with cartilage, hard margins and infiltrated bases. Typical (indolent) swelling of the retro- and submaxillary lymph nodes is an accompaniment.

The differential diagnosis from carcinoma may be clinically impossible. The author saw a case pronounced by dermatologists as a perfectly typical chancre, which proved to be a tonsillar carcinoma on section; erosion of the carotid caused acute fatal hemorrhage. On the gums, tonsils and pharynx, there occur as elsewhere in the oral cavity: (1) erythemas, with sharp demarkation of the red, slightly infiltrated, blue ringed areas; (2) papules or plaques as sharply circumscribed elevations of the character described before (p. 556); (3) gummas which disintegrate into ulcers, scars, perforations, and end in complete cicatricial atrophy of the tonsils.

Erythema of the mucosa appears, as a rule, with the first cutaneous syphilitic eruption, is usually stubborn, causes sensitive fissures and is very likely to recur within the first year after infection. It has been also called "erythematous syphilitic angina." It differs from simple angina, as a rule, by its mild swelling.

Gummas of the pharynx below the mucosa may reach considerable extent and cause deep ulcers; healing leaves very marked cicatricial adhesions between the posterior pharyngeal wall and the palate, dividing the pharynx into two separate cavities, the upper communicating with the nose and the lower with the mouth. Nose and mouth are completely separated, unless there is a perforated palate. Because of the great danger of contagion to other members of a family, Gerber calls particular attention to latent infection of the throat in this disease.

**Glanders.**—Acute cases are characterized by pustules and very progressive ulcers, while chronic cases develop infiltrations and torpid ulcers. The ulcers and their later scars which resemble scars of the skin due to burns, are not easily differentiated from luetic scars.

**Leprosy.**—The changes are similar to lepromas of the nose (p. 299), of the larynx, (p. 319), and skin (for details, see there).

**Actinomycosis** of the tonsils with subsequent cervical phlegmon is rare (Bostroem, Thevenot, Wright). On the other hand, actinomyces-like granules are found frequently in the tonsils, which gave rise to the assumption, formerly made and accepted, that actinomycosis of the tonsil was frequent, even without alterations (lit. by Gappisch, Miodowski, Jaehn).

For **scleroma** of the naso-pharyngeal mucosa, see p. 301.

In **typhoid fever** the follicles of the palate (Cahn), the tonsils and the pharynx may swell and ulcerate; hemorrhages are rare. In the second week of typhoid fever, quite shallow oval ulcers make their appearance bilaterally on the anterior palatal arches at their transition into the soft palate and also on the uvula in about ⅓ of the cases; they heal quickly or slowly without scars, usually in 1 to 2 weeks. They are not specific, nevertheless are spoken of as typhoid ulcerative angina. In rare cases, both in children and adults, an extensive gangrenous tonsillitis and gingivitis occur, also non-specific.

**Sporotrichosis** (see under skin) of the mucosa of the mouth and pharynx may be presented in the form of shallow and small, to very extensive ulcers with gray to gray yellow raised coatings. The cervical lymph nodes remain free (de Beurmann a. Gougerot, Milian, lit.).

### Tumors

**Benign.**—The soft palate and the tonsils rarely exhibit small fibromas, lipomas (lit. Imhofer), pedunculated, round, smooth and yellow (Glas,

Theisen, Sommer, lit.), chondromas, angiomas, so-called papillomas (fibro-epitheliomas), delicate berry-like tumors with arborescent, vascular fibrous matrix and thick epithelial coverings. Generally speaking, palate tumors are rare; those relatively frequent are the so-called endotheliomas (Volkmann, Eisenmenger, Looser) with pronounced tendency to hyalin or mucoid degeneration of the cells and the supporting substance (so-called cylindromas), sometimes containing cartilage, which relates these growths to the mixed tumors of the salivary glands (see fig. 104, p. 182). With others, the author believes in the epithelial nature of the essential elements of most of these tumors (epitheliomas, or basal cell carcinomas) (Malassez, Krompecher, Coenen, Clairmont, etc., comp. Ehrich). Clinically, they are benign, as a whole, encapsulated, covered by mucosa, slowly growing to the size of peas, almonds to oranges (Milian), do not produce metastases and do not return after complete removal (Spangenberg, Roach, Barbezat). Amyloid tumors (p. 323) are rare (Holmgren).

Cysts in the pharyngeal arch are considered due to cystic degeneration of the partially closed pharyngeal bursa remaining from embryonal time as an outward bulging of pharyngeal mucosa against the os basilare.

Rarely a cerebral hernia (inferior) bulges from the cranium and projects like a tumor into the pharyngeal cavity.

Naso-pharyngeal polyps grow downward into the pharyngeal cavity, mostly in young males, and nasal polyps hang down into the pharyngeal space (p. 303).

Almost all retropharyngeal tumors belong to the connective substance group. They may extend upward (base of cranium) in the posterior nares, less commonly, downward toward the larynx. Children are the most frequent victims (lit. by Brunner and Hellendall).

Congenital pharyngeal polyps, epignathus (parasitic), are rare tumor-like malformations showing all transitions from simple compound polyps to polypoid teratomas, to macroscopic parasitic doubles showing their character as an undeveloped twin by fetal organs, or body portions (asymmetric duplication). For this reason Schwalbe combines the several forms under the one heading of epignathus. They are differentiated into: (*a*) Simple congenital pharyngeal polyps, perhaps covered with skin and hair (hairy congenital pharyngeal polyps; lit. by Reuter, Levinger, Axhausen, Oppikofer) and consisting of a few simple tissues, such as fat-connective tissue, cartilage in mixed tumors; they are larger or smaller, easily removable and situated in the mouth, on the palate or its vicinity; (*b*) polypoid teratomas are the most frequent form of epignathus as shapeless, tumor-like masses covered partly with skin and partly with mucosa, and often of such dimensions as to impede delivery (illustr. by Simmonds); like

a polyp they are attached by a pedicle to the cranial base or to the palate. For this reason, Marchand calls them spheno- or uranopagus instead of epignathus. In most instances, they hang or force themselves out of the mouth. They are composed of derivatives of all three layers in a tumor-like mass, often containing numerous cysts with various kinds of epithelium including dermoid and epidermoid cysts, but not showing the organ-like structures that are reserved for the completed epignathus, which is a very rare tumor-like "parasite," suspended as in (*b*), but containing teratomatous structures and body portions immediately recognizable as developed organs, *e.g.*, lower extremities (Thellung, lit.). Schwalbe describes another, still rarer, still higher differentiated group of epignathi in which the funis of a second imperfect part of an individual, the parasite, is attached to the palate or its vicinity of the autosite; as a rule, the parasite is an acardius acephalus. Closely related to the epignathus is the encranius developed in the skull cavity by parasitic inclusion.

Sacral teratomas, or parasites, are considered equivalent to epignathi, being derived like these and other teratomas from separated cells of the embryonal autosite (comp. R. Meyer), blastomeres in complicated parasites, and cells of later development in simpler forms.

Arnold differentiated teratomas into: (*a*) those explainable by autochthonous displacement of tissue within the fetus; and (*b*) heterochthonous, requiring the assumption of a second unequal fetus. The first assumption may indeed explain simple congenital pharyngeal polyps, and is the simplest explanation for dermoid tumors and lipomas, as well as cholesteatomas of the cerebral pia mater.

Lipomas of the hypopharynx, of submucous origin (scattered primitive fat germ cells), very frequently assume the shape of a pedunculated polyp (lit. by Goebel).

**Malignant Tumors.**—Sarcomas, usually small or large round cell, sometimes occur on the palate, tonsils (where the author saw a round cell sarcoma with much karyokinesis the size of a plum in a 5 year old boy) or in the pharynx. Those in the latter situation may progress to the nose (observation of the author, p. 304) and infiltrate the cervical lymph nodes and muscles. They sometimes show a marked tendency to hemorrhage. Rare pigment sarcomas (or carcinomas) appear to be derived from pigment spots, observed by Eisenmenger on the hard and soft palates. Wagner and Mikulicz described a rhabdomyosarcoma of the tonsil, and Iwata described a teratoid tumor of the tonsil which, among other tissue, contained cross striated muscle fibres. Schmincke described malignant lympho-epithelial tumors (p. 604) in the tonsils with large cells, diffuse infiltrating growth, and reticular syncytial structure with thorough infiltration of lymphocytes. These "carcinomas" are easily mistaken for sarcomas.

Lymphosarcomas (p. 274) of exceedingly rapid growth, but only slight tendency to ulceration, may be derived from the lymphoid tissue of the palate and especially the tonsils, cause marked narrowing of the isthmus of the fauces, extend rapidly to the lymph nodes and infiltrate the tissues of the neck. Conversely, a lymphosarcoma from the cervical lymph nodes may extend rapidly to the palate and pharynx, infiltrating the latter in ridges or diffusely.

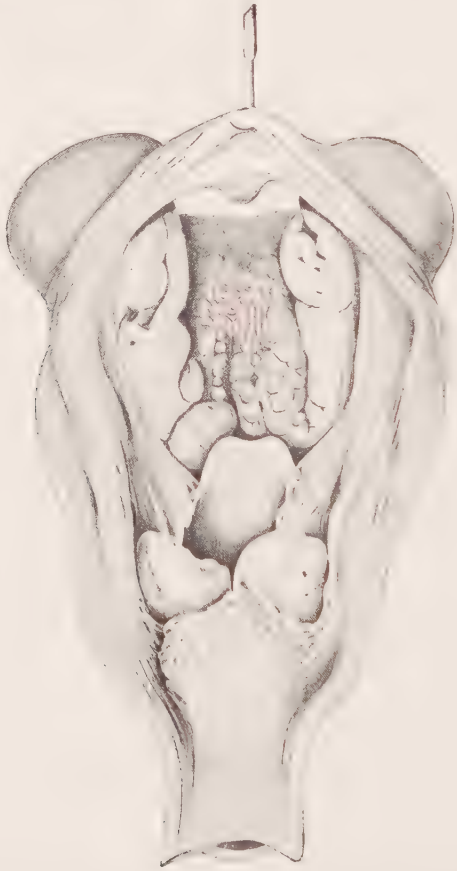


FIG. 277.—Aleucemic adenia (adenia simplex) of tonsils, lingual follicular glands and the laryngeal part of pharynx. There was also marked enlargement of the maxillary and submaxillary, axillary, inguinal, mediastinal, epigastric and retroperitoneal lymph nodes of moderately firm consistency in woman of 76 years of age, extremely emaciated (body length 153 cm., weight 29.79 kg., spleen weighed 277 gms.); $\frac{1}{5}$ nat. size.

In aleucemic adenia (p. 265) the adenoid pharyngeal ring (palate, tonsils, lingual base) and the piriform sinus may thicken into smooth or nodular, dense rolls or combs (fig. 277), while the cervical lymph nodes, finally those of many other localities, become enlarged.

In lymphogranulomatosis, participation of the pharyngeal adenoid ring is relatively rare.

Leucemia (p. 203), *i.e.*, lymphatic leucemia, may produce quite similar pictures. If the result of blood examination is unknown, the tonsils especially may suggest a primary malignant tumor when the infiltration extends or undergoes purulent necrotic disintegration (p. 559).

Plasmacytomas (pp. 272, 564, 573) occur in rare cases as diffuse infiltrates (lymphadenome diffus a plasma cells, Brocq and co-workers), or as a tumor (v. Werdt) in the palate, tongue and naso-pharyngeal mucosa; in an observation of the author (pub. by Kusunoki-Frank, lit.) the cervical lymph nodes were also changed. In a 30 year old man, the author saw a plasmacellular granuloma the size of a pea and arborescent, attached by a broad base to the tonsil. In another man of 30, the tonsil, appearing tumorous, showed the picture of plasmacytoma in the material excised.

Carcinomas, as a rule, of the squamous cell variety, may spring from the palate, tonsils, from the meso- and especially the hypopharynx. (The pharynx is the naso-pharyngeal space to the lower border of the cricoid cartilage. Three parts are distinguished: nasal, oral portion, laryngeal, or epimeso and hypopharynx. The latter is also called the pharyngo-larynx.) They grow quickly, ulcerate, bleed early, and endanger the larynx by direct invasion, by compression, or by acute laryngeal edema.

Tonsillar carcinomas are usually first recognized by hemorrhage and difficulty of deglutition and speech, or the enlarged tonsil projects more and more from its bed. Ulceration is early; the tumor grows at the peripheries while the ulceration goes deeper and deeper. Erosion of the carotid may terminate the condition.

In a 30 year old woman (medullary carcinoma) the author saw immense lymph nodes closely adherent to the jugular vessels and enlarged nodes in the axilla.

Metastatic carcinoma of the tonsil is very rare, and has been observed in carcinoma of the breast (Stoll, lit.) and carcinoma of the colon (lit. by Ribbert).

**Differential Diagnosis.**—The carcinomatous ulcer has overhanging, undermined margins and nodules in the base.

The ulcerating chancre shows sharply cut margins of almost cartilaginous firmness and bacony firm base. The indolent maxillary lymph nodes are less hard than those of carcinoma.

Disintegration of gummas leaves deep holes quickly enlarging with irregular edges as though stamped out.

Carcinoma of the lower part of the pharynx, especially of the piriform sinus is relatively rare (0.92% in 1078 cases of carcinoma at Basel).

The tumor is usually a hard ulcer, more rarely a lumpy or smooth fungus to the size of a chestnut. It presently invades the aryepiglottic

ligament, and displaces the epiglottis obliquely from the marked pull of the contracting carcinoma (fig. 278) which then progresses further into the larynx (fig. 278). This is spoken of as "external laryngeal carcinoma" (p. 324), but the laryngeal symptoms are often predominant. In fact, if

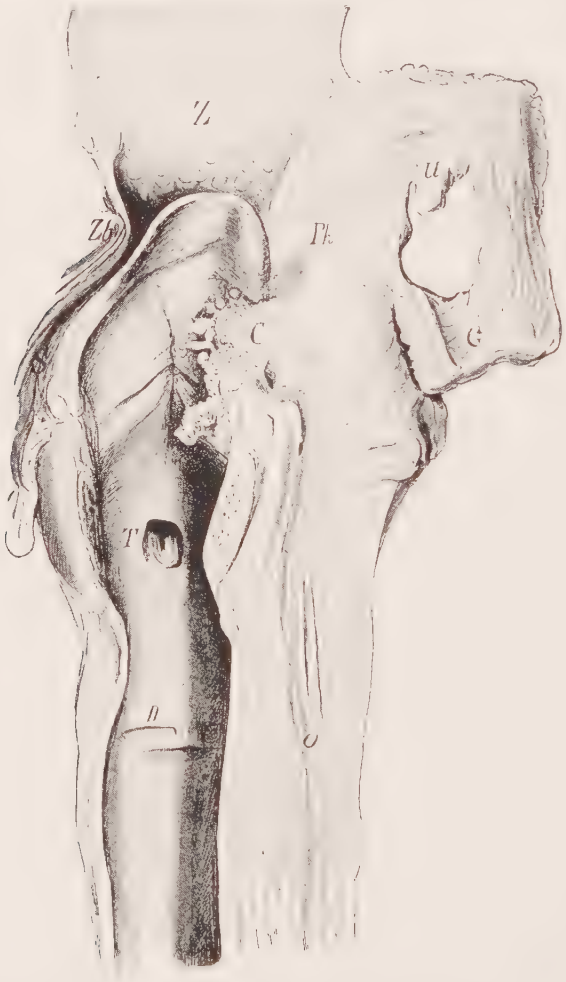



FIG. 278.—Scirrhous squamous cell carcinoma of right piriform sinus, (c) continuing to larynx. Rt. vocal cord at posterior attachment undergoing carcinomatous infiltration; on its middle portion lies a polypoid floating tumor mass; S, left piriform sinus; Zb, cornu of hyoid bone; Z, tongue; Ph, pharynx; U, uvula; G, soft palate; O, esophagus; D, decubital ulcers from the tracheotomy cannula; infiltration of submaxillary lymph nodes. Tracheotomy on account of acute edema of larynx (which is not visible now, but the left ary-epiglottic lig. is somewhat wrinkled). Death from gangrene of lung; ¾ nat. size.

the carcinoma is well advanced, it is very difficult to determine, even at autopsy, in the absence of a history, whether it was primary in the pharynx or larynx. The oblique position of the epiglottis, mentioned above, is

evidence of a pharyngeal tumor. Most pharyngeal carcinomas, even if small (Imhofer), cause quite enormous infiltration of the cervical lymph nodes and the author repeatedly saw crateriform perforations of the skin. They also cause deglutition, speech, and respiratory difficulties. The clinical diagnosis, as in esophageal carcinoma, may be misled by the "cervical tumor." Thus the author found an almond-shaped carcinoma of the left piriform sinus in a case of operated, clinically primary, cervical tumor, which was intimately adherent to the vagus.

Secondarily, the palate, tonsils and pharynx are frequently involved by both lingual and laryngeal carcinomas. Metastases may appear everywhere. In 10 cases, the author twice saw metastasis to the brain.

### Animal Parasites of the Buccal Cavity, Palate and Pharynx

Cysticercus occasionally occurs in the lips and tongue and during life gives diagnostic difficulties (see remark, p. 567).

Echinococci are rare in the tongue, cheeks and tonsils.

### Decubital Necrosis of the Pharynx (Fig. 279)

This is a pressure necrosis with prompt ulceration in the anterior wall of the hypopharynx on which the cricoid cartilage rests; usually there is also a necrosis on the corresponding posterior wall like an imprint of the first. In the beginning a yellow brown scab is seen, usually round, rarely angular (as in fig. 279), which is demarkated, detached, and leaves an ulcer. In the base of the ulcer is the plate of the cricoid cartilage, often calcified and showing perichondritis; it shreds, becomes necrotic, partly detached, or is expelled. In the base of the corresponding ulcer on the posterior pharyngeal wall, the vertebra may become visible. This condition occurs in very weak individuals because the larynx falls backward and rests on the spinal column in the dorsal position.

When the circulation is weak, this, at times, is sufficient to stop the circulation in the compressed areas and lead to death of tissue (decubital pressure necrosis).

Occasionally, a pressure necrosis of similar character may be produced by trauma, *e.g.*, during the passage of sounds, or wedging of solid food fragments.

That the development of decubital necrosis is favored by lordosis of the cervical spine (Koschier) is considered true by the author (con. F. Schw. 17, 1906). Extension to the cricoarytenoid point may fix the vocal cords and produce stenosis of the larynx, but acute edema is rare.

The author saw an unusual decubital necrosis in a 51 year old man who had died of pneumonia and who suffered with difficulties of deglutition. To the right was found an arytenoid perichondritis with angular

projecting arytenoid cartilage and its imprinted ulcer to the right on the lateral pharyngeal wall. The cartilage of Santorini was absent. The inside of the larynx showed no changes. There are still other atypical forms; the author saw deep ulcers to the size of a cent with thick rounded edges only on the posterior pharyngeal wall, caused by the hard angular prominent cricoid cartilage, while the mucosa over the cartilage was intact.

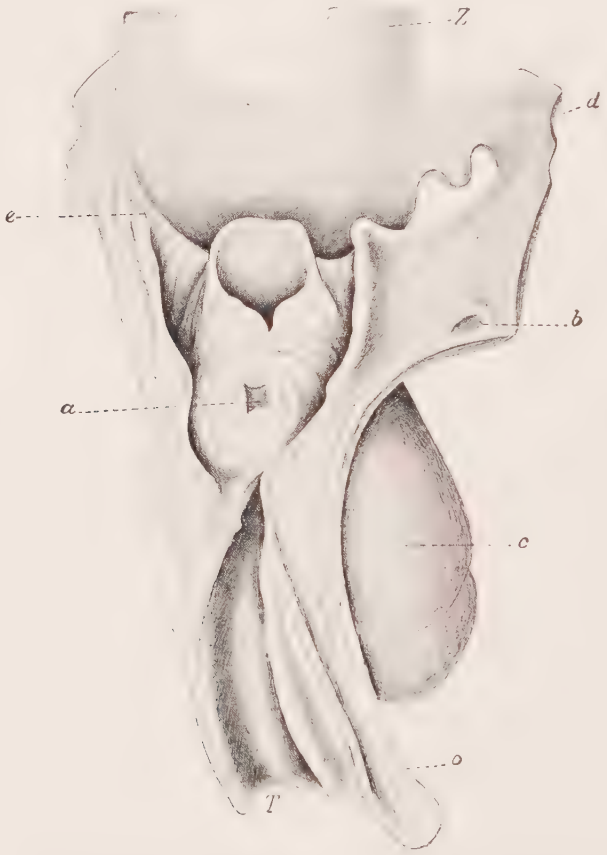



FIG. 279.—Decubital necrosis of pharynx; a and b, symmetrical ulcers on anterior and posterior wall of pharynx; at the base of a, the exposed annular cartilage; quite marked goiter (c); d, palate; e, left greater cornua of hyoid bone; Z, tongue. Pharynx cut open laterally and turned to the right; O, esophagus; T, trachea; the former opened laterally, the latter in middle. Edema in lower part of ary-epiglottic folds (so-called edema of glottis); woman 39.

### Mouth and Pharyngeal Structures in Poisonings

Compare chapter on corrosions of the esophagus, p. 638, and stomach, p. 672.

Corrosive action on the oral and pharyngeal tissues by fluids is not deep, as a rule, on account of the short time of contact. Usually there is only an inflammatory reaction, but necrosis of epithelium, and at

times pure pseudomembranous inflammation, do occur. Sometimes the corroded areas show a characteristic discoloration.

According to Kolbert, (1) corrosive alkalies potassium and sodium hydroxide cause corrosion and white discoloration of the mucosa of the mouth; ammonia causes swelling and blisters. (2) Corrosive acids: sulphuric, external brown crusts, in the mouth, gray white detachment; nitric acid in solutions over 30% yellow corrosion of lips, mouth, pharynx; hydrochloric acid: corrosion and white discoloration of the mouth and pharynx. (3) Heavy metals, *i.e.*, their corrosive salts, mercury (sublimate and red oxide), black edges on gums, glossitis. (The same effect occurs even if the mercury is not taken by mouth.) Silver, as the nitrate, leaves white scabs in the mouth; copper, as the sulphate in acute poisoning, green eschars in the mouth; zinc, as the chloride in acute poisoning, the mucosa is bloody or white and wrinkled.

Poisoning by lead and bismuth: lead, white gray discoloration, lead line; bismuth, black staining of the gums and other changes. No local corrosive effect, only the expression of a general intoxication as in mercury poisoning.

For **diverticulae** of the pharynx, see under esophagus, p. 653.

## ESOPHAGUS

**Anatomy.**—The wall of the esophagus consists of three chief layers: mucosa, muscularis with inner circular and outer, longitudinal layers, the thickness increasing toward the cardia, and tunica fibrosa. The muscularis mucosae and submucosa separate the first two layers. The upper part of the esophagus also contains cross striated muscle fibers. The mucosa is covered with stratified squamous epithelium which produces keratohyalin; in the embryo it has cilia up to the 18th to 32nd week, first on the cylindrical, then the "metaplastic" squamous epithelium (E. Neumann); it also contains mucous glands grouped in twos and threes in interrupted longitudinal rows beneath the muscularis. These are small and grape shaped and number 200 to 300; two-thirds of them are found in the upper half (Schaffer). In the lowest portion we find the so-called lower cardia glands analogous to the glands found at the cardia. In the upper esophagus gastric mucosa islands also are present resembling erosions, as elongated, oval, somewhat elevated, brown yellow or gray yellow, sharply demarkated spots. At times they form paired aggregations and may reach the size of the nail of the little finger, but usually are small with slight indentations, often arranged symmetrically in the lateral recesses of the esophagus. Microscopically, they are covered with cylindrical or squamous epithelium and consist

of branching tubular glands surrounded by lymphoid tissue; they have chief cells and lining cells like the gastric cardia glands; they lie in the mucosa propria above the muscularis mucosae. Glinski found them macroscopically in 3% to 6% of autopsies, Schridde in 15%, Schwalbe-Lubarsch in 13%, and microscopically in 50%. He calls them upper esophageal fundus glands. Ebert thought them misplaced gastric epithelium; Schaffer (lit.) found them in 70%, called them upper cardia esophageal glands and believes they are developed when the esophageal epithelium, undifferentiated in its earliest stage, fails to change into ciliated cylindrical epithelium in these places but changes to gland epithelium instead. This is heterotopic development of gastric glands (comp. H. Hildebrand, Ruckert). Following more extensive investigations, Schridde himself rejected his theory previously held untenable by Schaffer and Keibel that the final lining of the esophagus came from downward growing ectodermic epithelium and where it failed to grow, the islands persisted as rests of the primitive entodermal esophageal lining. Now according to Schridde, the entodermal epithelium of the esophagus produces all cell forms which appear in the course of esophageal development as, for example, ciliated cells, mucous cells, cylindrical cells, squamous epithelium and fiber cells which are the definitive permanent cells of the esophagus; a certain kind does not simply transform itself into another (direct metaplasia) but each develops by differentiation from the basal cell row (original entodermal cells). The esophageal mucosa acquires its complete development only at time of birth and after. Schridde believes the first anlage of the islands are laid down at that time, *i.e.*, cylindrical cells grow in determined places from the basal cells and gastric glands evolve by differentiation. Nakamura believes that little cysts spring from these islands and he has described microscopic tuberculous changes in them.

The esophagus is 25 cm. long (cervical portion 5, thoracic 17, abdominal 3 cm.). The distance from the teeth to the cardia (level of 11th thoracic vertebra) is 40 cm. The distance from the teeth to the beginning of the esophagus (intervertebral disc between the 6th and 7th cervical vertebrae or correspondingly, the upper edge of the cricoid cartilage) is 15 to 17 cm. The esophagus and the left bronchus cross 25 cm. behind the teeth, or 8 cm. below the upper end of the esophagus.

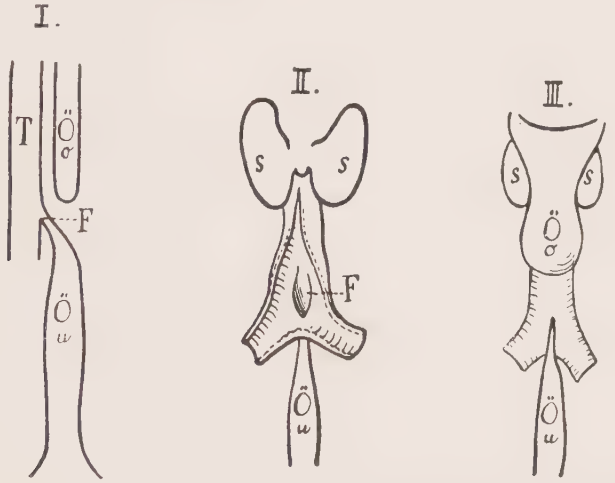
For the lymphatics of the esophagus, see p. 646.

### Congenital Malformations of the Esophagus

These are rare.

**Agenesia,** or absence of the esophagus with blind mouth and stomach ends connected by a thin strand of muscle, is very rare, but has been seen

in the severest abnormalities. Esophago-tracheal fistulae, persistence of an abnormal, broader or usually fine communication between the esophagus and trachea, due to disturbance of the separation of these parts, without other malformations, are very rare. Ciechanowski and Glinski described congenital esophageal fistulae in small children such as tracts or accessory canals situated in the anterior wall, with an upper and a lower opening. While these authors consider such fistulae malformations, for which they supply a complicated explanation, Sternberg, with Lotz, thinks they are merely dilated ducts of mucous glands changed into cysts and canals, and perhaps in part eversions of surface epithelium. These formations which lie in the submucosa are supposed to favor the development of phlegmonous esophagitis.




FIGS. 280 to 282.—Congenital atresia of esophagus with esophagotracheal fistula. I. diagram. T, trachea; Oo, upper; Ou, lower portion of esophagus; F, fistula. II. half-diagrammatic, anterior view. III. posterior view; S, thyroid.

The almost typical esophagus atresia with an esophageal fistula is not so rare. The esophagus is interrupted by a blind end at the upper portion, sometimes sacculated and dilated, and corresponding to the upper third (pharyngeal part) of the esophagus, while the lower section, sometimes funnel shaped and pointed, opens at its upper end into the posterior tracheal wall (above the bifurcation). The upper and lower portions are usually united by a tendinous muscle cord lying on the trachea. Forssner explains it in this manner: first an esophago-tracheal fistula is developed (see above); failure of the separation process probably is the chief factor in the complete epithelial occlusion above the fistula, and this occlusion in turn brings about the atresia. The lower esophageal portion without any connection with the blind upper end, seldom empties with a non-decreas-

ing lumen into the trachea (Latwig, lit.). Such children, perhaps well developed, but in many cases otherwise deformed (Gutmann), die of inanition (thirst), lack of oxygen, or aspiration pneumonia. Since no amniotic fluid was swallowed, the meconium contains no lanugo hairs (lit. by Happich, Giffhorn, Kern, Konopacki). A picture somewhat resembling this malformation may be developed by suppuration of lymph nodes, situated between the esophagus and trachea resulting in cicatricial occlusion of the upper part of the esophagus, while the lower part communicates with the trachea. More rarely the upper end of the esophagus enters the trachea. A simple blind end of the esophagus is rare, (Kraus); cases are more frequent in which the blind, tubular or funnel shaped affair is a diverticulum from the esophagus toward the bifurcation. In reference to their characteristics see under traction diverticulae, p. 652.

Stenosis, a congenital circumscribed narrowing of the upper or lower segment, or a congenital circumscribed dilatation (a form of anterior stomach), is very rare. Duplication of the esophagus (diesophagus), that is, two esophagi, with separate cardia entering the stomach is exceedingly rare. Kathe described a partial duplication, but this case may be interpreted differently as a fistulous tract remaining from an esophageal phlegmon (the author, Kopp, Lotz) or a congenital esophago-esophageal fistula (Ciechanowski and Glinski, see p. 631). Pharyngeal diverticuli on p. 653.

### Esophagomalacia

Cadaverous softening of the esophagus is produced by the entrance of gastric juice and subsequent digestion, (esophagomalacia acida). The epithelium is first macerated and dissolved, then the wall liquefies and may perforate, allowing the gastric juice to enter the pleural cavity. Slight degrees are often seen, as focal losses of epithelium in places corresponding to the longitudinal folds of the contracted esophagus, or severer degrees in complete detachment over greater distances.

Intravital esophagomalacia over larger areas is rare. Mild degrees are not rare; microscopic evidence of inflammatory changes (cellular infiltration, fibrin, hemorrhages, etc.) must be found if the condition is to be considered intravital.

Isolated cases have been reported (lit. Glockner Cantieri, lit. and illustr. Watson) in which circular ulcers were found in the lower esophagus, sharply demarkated from the stomach. This form of ulcer should be called "digestion ulcer" (Quincke). The author saw a case in a 78 year old man with hepatic cirrhosis and varicosities of the lower esophageal veins, some freshly thrombosed. The picture was that of a dark red, softened portion which stopped about a finger's breadth below the cardia

in a sharp zig-zag line; it reached like a belt a hand's breadth upward around the esophagus, suggesting escharotic action, which, however, was excluded on the basis of chemical investigation (Kreis). The essential factors in the malacia of this case were the circulatory disturbances of hepatic cirrhosis, the varicosities, the thromboses, bleeding into the wall, and hemorrhage on the free surface; 250 cc. of brown red turbid fluid had passed from the softened esophagus into the left pleural cavity. The stomach was empty, except some trace of substance similar to coffee grounds. The colon contained much tarry material.

Simple ulcers (peptic) are analogous to those in the stomach, so, also in rare cases, typical hemorrhagic erosions. In the lower part of the esophagus loss of substance can be seen in sharply circumscribed areas, brown in color, punctate to bean size, running more or less longitudinally, sometimes arranged in parallel rows, superficial, or invading the mucosa. They are often very numerous. As in a specimen in Basle (girl of 20 died after extensive burns) the adjacent mucosa is undermined.

### Circulatory Disturbances

Active hyperemia occurs at the beginning of various inflammations. Edema, especially of the lower esophageal segment, is often a consequence of vomiting according to Rost, but it is frequently inflammatory in suppurative peritonitis.

Passive hyperemia is most frequent in cardiac and pulmonary disease; hemorrhagic erosions (see above) also occur.

The veins of the esophagus form two plexuses; one, submucous, and one periesophageal; they have two outlets: those in the lower portion (1) through the intercostal veins to the azygos, those in the upper portion (2) via the vena thyroidea inferiore into the superior cava. In occlusion of the portal vein the azygos is an imperfect substitute and hemorrhagic congestion in the esophageal plexus is a result (see under liver).

Varices are rare in the upper part in the form of small blue nodules or sacculations or vermiform blue striae, in advanced age or congestion of the superior cava, as for example, from malignant goiters. In the lower part, varices are due chiefly to cirrhosis of the liver, portal thrombosis and not uncommonly luetic lobulated liver (very rare without liver changes); the phlebectasias or varices are in the submucosa and the outer wall, even as large as a lead pencil. Those of the posterior lower part are especially subject to rupture, perhaps from trauma during swallowing and may lead to fatal hemorrhage.

Vomiting of blood in younger individuals is sometimes the first and only symptom of cirrhosis of the liver (Zelensky).

It is remarkable how small, almost invisible, the perforations may be in fatal cases; for example, in a man 41 years old (cirrhosis of the liver with carcinoma—spleen 312 gms.—fatal hemorrhage in about 6 hours), the author saw three openings the size of pin-pricks in the mucosa; one, admitting the finest bristle, led upwards into a submucous varix on the posterior wall directly above the cardia. A similar condition is shown in a specimen from a luetic girl 26 years old with lobulated liver; in the anterior wall only one fine opening was found 1 cm. above the cardia; the same condition was found in another case of lobulated liver with fibrous peripyelophlebitis in a 25 year old man with a clinical diagnosis of chronic splenic tumor (spleen 960 gms.). In a luetic woman of 35 with lobulated liver (spleen 720 gms.) the opening was situated on the posterior wall 4 cm. above the cardia; it was rounded, sharp and the size of a hemp seed, leading into a submucous vein the size of a knitting needle. Occasionally a number of rather long oval openings several mm. in size are seen; these are arranged in a row and admit a fine probe.

Congenital varices and hemorrhages are rare (Vorpahl).

Larger hemorrhages occur also from injuries, tissue loss and ulceration and the hemorrhagic diatheses such as pernicious anemia and typhoid fever (Rossle). Usually the larger vessels in the vicinity of the esophagus and not the esophageal vessels themselves, except possibly in carcinoma, are the source. Foreign bodies may perforate the aorta or an aneurysm of the aorta may cause pressure atrophy of the esophageal wall and rupture into the esophagus, with vomiting of bright red blood; or conversely the esophagus may rupture into the aorta and other vessels (pulmonary, carotid and inferior thyroid arteries, left auricle, etc.) from trauma and ulcerations, especially carcinomatous.

In an extirpation of a pharyngeal carcinoma in a 32 year old man, the right subclavian artery which coursed abnormally from the left towards the right, behind the esophagus, had been injured by the pressure of a gastric probe which was left for several days, being inserted for "dysphagia lusoria." Fatal hemorrhage resulted. This variation of the right subclavian artery which begins as the last branch of the arch of the aorta is not so rare, but does not always cause dysphagia lusoria (Rossle, Mouton).

Punctate or petechial hemorrhages occur occasionally in the hemorrhagic diatheses (pernicious anemia, anemia, leucemia), sometimes also in typhoid fever.

### Inflammations

**Simple Acute Catarrh.**—Because the glands of the mucosa are few in number, little secretion takes place, but much epithelium is desquamated

(desquamative catarrh). The mucosa is hyperemic. Catarrh may be caused by irritation from food and drink, by continuity from the pharynx, and various infectious diseases.

Birch-Hirschfeld described a case of total, rapid desquamation of the whole epithelial coat of the esophagus in the form of a connected tube (exfoliative esophagitis or superficial dissecting esophagitis). Exfoliation was caused by an exceedingly acute epithelial suppuration, etiologically obscure in a hysterical woman, otherwise healthy. In a specimen in Breslau the exfoliation was due probably to scalding. In a specimen in Basle (28 to 30 cm. long vomited by a man 42 years old) the translucent tube, folded longitudinally shows innumerable minute bosses (imprints of papillae). A 64 year old woman after a pharyngitis vomited a 30 cm. long epithelial tube; the author found the lower layers infiltrated by round cells. Stern saw similar conditions. In a case of Sclavunos exfoliation occurred after ingestion of strong spirits. This must not be mistaken for an expelled tube of necrotic mucosa (deep dissecting esophagitis) observed after corrosion from acids and alkalies (lit. by Grau). The author examined a tube expectorated after drinking lysol, 23 cm. long, externally corresponding to the infiltrated submucosa; it was felted, inside smooth and necrotic; death of the 48 year old woman, two months later from inanition (total stenosis of the esophagus) (pub. by Winter).

**Chronic Catarrh.**—This is usually found in the congestion of cardiac and pulmonary diseases, also in drinkers and in the dilatations above stenoses. The mucosa is hyperemic, blue red, the epithelium thickened in longitudinal stripes or in the form of flat blue white blotches (leucoplakia). In older cases the mucosa is thickened, striped, or polypoid and covered by thickened epithelial layers (fig. 283). The latter macerates in the cadaver often in rags which hang together. The musculature may become flabby causing dilatation, but it may also hypertrophy causing a shelved appearance on cross section.

The striking and frequent relation of leucoplakia to carcinoma as in the buccal cavity is almost unknown in the esophagus, but Fuzii thought he demonstrated a beginning leucoplakia carcinoma (basal cell).

Chronic catarrh also develops in spastic stenosis (comp. chapt. VIII) and the stenosis of paralysis due to destructive cerebral, medullary and cervical spinal cord processes, vagus compression or intoxication from alcohol, lead, etc.

So-called follicular catarrh, follicular esophagitis (Chiari) or cystic esophagitis is developed when the relatively few mucous glands (p. 629) participate markedly in the inflammation. The ducts are blocked by secretion; small retention cysts are filled with glassy mucus and occasionally reach the size of a pea. Round cell infiltration occurs around the

glands and if marked, suppuration, erosion and ulceration may set in sometimes followed by phlegmons. Nakamura doubts that cyst formation is due to inflammation, and he would have the conception of cystic esophagitis discarded for simply cysts of the esophagus; the proposition could be investigated experimentally.

**Pseudomembranous and Necrotizing Inflammations.**—The superficial fibrinous or croupous and the deep or diphtheritic (necrotizing) forms are rare in the esophagus and are chiefly by continuity from the pharynx. They occur occasionally in the severe infectious diseases (scarlet fever, typhoid fever, cholera, etc.) and other ailments, as for example, uremia. The gray yellow coating of fibrinous esophagitis in stripes, corresponding to the apices of the folds, or as tubes over the whole surface, has a certain resemblance to oidium albicans infection (pp. 560 and 657).

Pseudomembranous inflammations may also be caused by escharotic poisons and thermic influences.

True diphtheria (in a clinico-bacteriological sense) is very rare, (Ceelen), and usually fatal. Ordinarily the esophagus is fairly immune to the diphtheria bacillus, but the stomach is often infected, especially if its secretion is inhibited by the fever (Grunfelder).

Deep streptococcic esophageal necroses, corresponding to those in the tonsils and palate and occurring with others in the gastric wall, were described by E. Fraenkel, etc., in scarlet diphtheria. The author has seen this repeatedly; in a 6 year old girl the inner surface of the thickened dilated esophagus was covered to the cardia by lesions, mostly striped, reaching into the submucosa, and suggesting corrosion. In a second case there were two circular ulcerative lesions several centimeters in length reaching to the muscularis (4 other cases by Schick, I Diss. Basle, 1907). Cicatricial strictures may result (lit. by Oppikofer). Small focal necroses over the whole mucosa were seen in scarlet fever, and also in a child with facial erysipelas.

**Pustular Inflammation.**– In small pox (see under skin), papular eruptions appear in the mucosa, the epithelium is cloudy, thick, loose and frequently exfoliates, leaving ulcers.

**Phlegmonous Inflammation.**– Purulent infiltration begins in the submucosa; the mucosa becomes hard, stiff, thickened and bulging (up to 1 cm. in thickness), undermined (deep dissecting esophagitis), perforated, often like a sieve, the perforations chiefly in the long axis. If the suppuration extends to the vicinity (phlegmonous periesophagitis) it may eventually perforate into the larynx or trachea, mediastinum or pleural cavity.

**Etiology.**—The phlegmon may be a direct continuation from the pharynx, or may be caused by foreign bodies (swallowing false teeth, etc.), escharotic poisons, other irritating substances (alcohol) in conjunc-

tion with invasion of pyogenic organisms. It is also produced by continuity from the neighborhood (perichondritis of the larynx, vertebral caries, suppurating caseous tuberculous nodes, carcinomatous lymph nodes) to the outer layers of the esophagus; the periesophagitis then spreads chiefly in the submucosa. Continuity from the cardia is rare, although seen occasionally in drinkers. The author saw it follow a gastric phlegmon, due to an operative gastro-enterostomy (p. 669). Cystic esophagitis may be a starting point of phlegmonous esophagitis (p. 635; Sternberg).

Phlegmon of the esophagus is usually fatal in 8 to 14 days; if healing occurs, cavities are left containing strands and communicating with the lumen through several, often very tiny holes. These intraparietal cavities and channels lined with epithelium are of no consequence as a rule, even though their meshes seem to be especially well adapted to retain ingesta, or arrest probes during examinations, etc. Literature of phlegmonous esophagitis by Joliat.

### Infectious Granulation Tumors (Rare)

Tuberculosis occurs in the form of angular or rounded, arched, circumscribed, shallow, lenticular, or crateriform ulcers, rarely leading to stenosis by cicatricial contraction (K. Zenker). The ulcer bases frequently contain caseous lymph nodes which communicate the process to the esophagus and from which fistulae may develop; occasionally, the process comes from a prevertebral cold abscess in vertebral caries. Cases are seen in which a traction diverticulum had been produced by anthracosis of lymph nodes, and this became involved in tuberculous infection from the neighborhood. Smaller lenticular ulcers can be seen in the vicinity of larger ulcers, thus developing annular stenosing infiltrations (rare). In other cases such relations to lymph nodes are absent, and the infection is of hematogenous or lymphogenous origin, or (in superficial ulcers) an inoculation from swallowed sputa, especially when there have been previous corrosions (Chiari, lit.) or thrush infection (Eppinger) or carcinoma (Zenker). Hematogenous miliary tubercles, chiefly in the musculature, are very rare (Glockner). In the presence of an ulcer, the musculature may be sprinkled over large distances by many lymphogenous miliary tubercles (rare). In one case the author saw yellow, flat, caseous foci in the walls from perforation of a caries of the vertebra into the esophagus. According to Glinski and Nakamua, the islands of gastric mucosa (p. 629) may also become infected by tuberculosis. Extension of tuberculous ulceration from the larynx and pharynx to the first portion of the esophagus is not rare, but deeper descent is rare (lit. in appendix).

Syphilis is seen in the form of ulcerative disintegrating gummas which may (rarely) lead to perforation into the trachea, etc.; and in the form of constricting scars from healed gummas, chiefly in the middle portion; syphilis is rare (lit. by Kraus).

Actinomyces may enter the body primarily from the esophagus, as, among others, the case of Soltmann shows, in which a grain of infected barley was later evacuated from an abscess of the back. Nodules and ulcers, rarely tumor-like lumps, are the anatomical forms (lit. by Garde, Abbee, v. Baracz). Further extension from the periesophageal tissue (prevertebral phlegmons) occurs in the manner described, p. 469; see p. 466 in reference to involvement of lungs and pleura. The esophagus may be secondarily involved by actinomycosis of the thorax or lungs.

### Corrosion of the Esophagus

These are frequent and important because of the severe suffering from subsequent strictures. Escharotic poisons produce inflammations, necroses, or both (cf. under stomach, p. 672). Dilution usually determines an inflammation, concentration a necrosis, the degree depending on the strength of the poison and the duration of its action. The severest changes occur on the apices of the longitudinal folds of the mucosa because of strong contraction of the muscularis. In superficial corrosion the epithelium undergoes necrosis and covers the injected mucosa with a cloudy croupous membrane; in severer damage the deeper layers of the wall also become necrotic (encrusted). Edema appears around the necrosis and demarkating suppuration; sequestration of the scab, rarely in the form of a long tube (see observ. p. 635) leaves an ulcer and hemorrhages. After slight corrosion, the epithelial regeneration produces perfect healing; severer degrees heal by granulation to annular scars, often of immense thickness and remarkable length, in fact, throughout the esophagus. The subsequent strictures may become impermeable, and are followed by dilatation and hypertrophy above.

The physiological narrow regions of the esophagus help decide the localization of annular corrosions (comp. statement p. 642), (v. Hacker, Mehnert).

Compare p. 629, in ref. to corrosive poisons, p. 636, under deep dissecting esophagitis and under stomach.

### Cysts. Tumors

**Cysts.**—There are (1) rare ciliated epithelial cysts, chiefly in the lower portion, reaching the size of an apple, according to v. Wyss and Zahn, originating from snared off embryonal structures, when the epithelium was still ciliated and cylindrical, but according to Trespe, who found

cartilage in their walls, arising from the pharynx. Bert and Fischer extend the conception to include the so-called ciliated epithelial cysts of the mediastinum which they call esophagus cysts, while Gold considers such structures derived from rudimentary or cystic accessory bronchi, calls them bronchus cysts and classifies them as malformations of the lung. Staehelin-Burckhardt (lit.) described an esophageal cyst containing gastric mucosa (p. 629), (Mohr, Stoeber, Pappenheimer, lit.). (2) Small multiple retention cysts of the ducts and mucous glands occur, especially in the upper part of the esophagus (Kuhne, Kern, Nakamura, lit.; for another conception, see Landois). (3) Sometimes small cysts start from the islands of gastric mucosa (Nakamura). (4) See follicular or cystic esophagitis, p. 635.

**Benign Tumors.**—They are rare and usually unimportant.

There occur polypi and papillomas of the mucosa; the former, perhaps with long pedicles, are smooth mucous hyperplasias covered by epithelium; the latter are papillary fibromas, sometimes vascular with a tendency to hemorrhages.

Adenomas, with pancreas-like lobulation and of small size, are very rare, likewise internal and external leiomyomas and fibromyomas (lit. Frank) usually on the anterior wall in the lowest segment or at the level of the bifurcation to the size of a bean, rarely larger (size of a plum, Bauer), sometimes annular and stenosing (Anitsch-Kov); lipomas are usually very small nodules in the submucosa; if larger they become polypoid and pedunculated due to pulling during deglutition.

**Malignant Tumors.**—Primary sarcomas are very rare, favor the male sex, especially in advanced age and begin chiefly in the lower third. Spindle, round, and polymorpho-cellular, very rarely lymphosarcomas, and even melanotic sarcomas (Baur) have been observed. Their starting point is chiefly the submucosa; they may quickly reach large dimensions, compress the trachea and cause edema of the larynx. They are circumscribed, nodular, pedunculated, polypoid, firm, smooth and covered by mucosa or diffusely infiltrating, softer and massive, usually undergoing gangrenous destruction; the latter sometimes produce metastases even in the skeleton and brain, may extend to neighboring organs, and pleuritis, pulmonary gangrene, eventually perforation of the esophagus, may follow. Macroscopical differentiation from carcinoma may be impossible, also true of similar tumors of the stomach (lit. by Starck; also clinical matter Borrmann, Herxheimer, Donath, and especially v. Hacker). Wolfensberger described a large polypoid rhabdomyoma (metastases in lymph nodes); a similar tumor, size of a hen's egg, was described by Glinsky, (location lower portion in men 68 and 75 years old respectively). Carcinoma and sarcoma combined (carcino-sarcoma) are described by Fragen-

heim (lit.), Herxheimer; carcinoma and sarcoma, separately by Reith. There are also carcinomas with merely a "sarcoma-like" stroma (Herzog); Schlagenhaufer (lit.) saw a secondary lymphosarcoma; see literature in appendix.

Carcinoma is frequent and of great importance. It is almost always a squamous cell tumor starting from the epithelium with frequent "onion

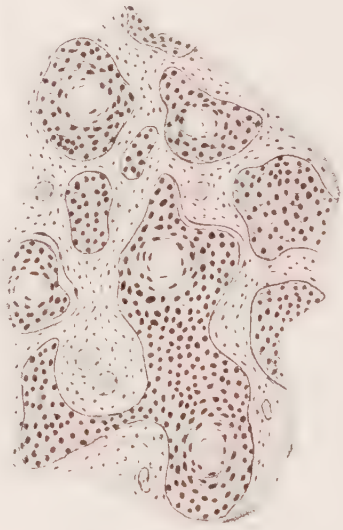


Fig. 284

Fig. 283.

Fig. 283.—Constricting annular carcinoma of esophagus, (scirrhus) in lower part (c); above, spindle-shaped dilatation; marked hypertrophy of muscularis (inner layer). Chronic esophagitis with thickening of epithelium (leucoplakia) in dilated portion. Below the carcinoma is the cardia of stomach; $\frac{1}{5}$ nat. size.

Fig. 284.—Cornifying scirrhous squamous cell carcinoma of esophagus; (med. magn.).

skin" stratifications and cornifications similar to many carcinomas of the skin (cornifying squamous cell carcinoma).

The size of the tumor groups and the cornification are quite varied; there are small and large islands, far apart or close together, with corresponding hard or soft textures. The polymorphism of the cells and the amount of chromatin in the nuclei also vary considerably.

Some tumors are baso-cellular, usually the simpler forms are of this type, (see under skin), but the author has seen cylindromatous pictures. Transitions also occur into cornifying squamous cell tumors. Others, non-cornifying, consist of small, rounded, angular cells (round cell carcinoma) in small, or large groups, soft, medullary, voluminous, fungoid with tendency to necrosis, fatty degeneration and gross disintegration. The interstitial tissue of the granulations may show much small cell infiltration which obliterates the margins of the islands; or in scirrhous forms, the tumor is fibrous and very hard.

Cylindrical cell carcinomas, from gland epithelium or possibly from heterotopic gastric glands (p. 629), sometimes mucoid in structure, are rare (Hanot and Parmentier, Chavannaz, Fischer, Franke). The author saw both a scirrhous and a polypoid cylindrical cell carcinoma of almond size in an 85 year old man. Cornifying squamous cell carcinomas have been known to produce mucoid metastases; see the observation of the author mentioned under secondary carcinoma of the liver.

Most carcinomas show a tendency to extend annularly and produce stenosis. The insular carcinoma of the wall is rarer; it occurs as an ulcerated infiltration or as a projecting smooth button, or an elongated oval plateau, or fungus, chiefly on the anterior wall. Some carcinomas are soft, of prolific growth, and disintegrate soon into irregular, suppurating ulcers (fig. 285); others are hard, scirrhous, much less cellular, showing marked connective tissue development. Scirrhous forms are often of small extent, but cause the most marked stenoses. Those forms which are macroscopically shallow, like a simple ulcer, are very rare. The extent varies between 2 to 10 cm., rarely larger, and as large as the whole length of the esophagus (Caesar). Usually there is only one focus, but sometimes there is a chief growth and important accessory foci; secondary small foci on the other hand, are frequently disseminated in the vicinity of the main tumor, or submucous, in chains in the longitudinal direction distributed by the lymph channels.

In rare cases, two or more apparently independent isolated foci are found seemingly separated by healthy tissue; these must be carefully investigated to discover lymphatic contact and origin of one from the other which is the case in most instances. In cases with external lymph nodes uninvolved and separate tumors, Borrmann thinks that parietal metastasis by way of the blood may have occurred.

An esophageal squamous cell carcinoma is occasionally found simultaneously with a gastric cylindrical cell carcinoma. The author saw two such cases. In another case (42 year old man) there was an esophageal carcinoma with metastases to the liver, and a carcinoma of the left heel with metastases to the left inguinal nodes.

There are three sites of predilection of esophageal carcinoma: (1) the lower third, just above the cardia, and since these tumors progressively invade the stomach, they give the impression of primary carcinoma of the cardia; (2) the middle third, at the crossing of the left bronchus, (fig. 287); (3) the upper third, the pharyngeal junction; the lower and middle thirds are most favored. In 184 of the author's cases (from Breslau, Basle, Gottingen), the locations were upper third, 31; middle third, 61;

FIG. 285.—Big ulcerative carcinoma of esophagus of man 40 years old. The carcinoma had perforated into the trachea; 3/8 nat. size.

lower third, 84; in 857 cases from the literature, Kraus found 158 upper and 699 middle and lower thirds; (cf. Wendland, Calderara).

Perhaps it is of etiological importance that the esophagus is relatively narrower in the places named. These three areas (narrowest at the level of the cricoid cartilage) (mouth of the esophagus, Killian) are not the only narrow places; according to Mehnert, there are about 13, about 2 cm. distant from each other, physiologically but inconstantly appearing, corresponding to the number of intervertebral cartilages, *i.e.*, the idea sup-

ported by Mehnert and disputed by others (Happich) of the segmental structure of the esophagus. The most frequent narrowings are: cricoid cartilage, aortic narrowing at the bifurcation, at the left bronchus and at the diaphragm.

Larger food fragments meet a certain resistance, and may possibly cause chronic irritation favoring the development of carcinoma. Projections in spondylitis deformans, narrowing the passage, may act in a similar way (Zahn, Wolf). Foreign bodies, heat effects, the chronic irritation caused by alcohol, spicy foods and tobacco have also been held responsible. For the relation of leucoplakia to esophageal carcinoma, see p. 635. It is undeniable that drinkers show a certain predisposition. Traction diverticuli (p. 652) may be the starting point according to Heller-Arndt, Ritter, etc., and the author, the tumor developing at the edges or in the depths. In a case observed by the author (76 year old man) a small, long, oval, isolated tumor, shaped like a flat dish, was located on the anterior wall of the esophagus; the center of the pale gray red carcinoma showed a long depression of slate gray color which, diminishing funnel-shaped, ended in an anthracotic, chalky bronchial lymph node over the right bronchus. Carcinoma develops but rarely in the depths of a pulsion diverticulum (Huttner), or as the author saw, on its inner surface, lined with a white, poultaceous cornified carcinoma, or at its entrance, as the author saw in a 58 year old woman. v. Grabowski attempted to find a relation to the epithelial rests of esophago-esophageal fistulae mentioned on p. 631. Leucoplakia (Guisez), although the author never saw such a case, scars, tuberculous ulcers, etc., may also supply the base. Men are much more frequently attacked than women; in 130 cases in Basle the author found 10, in 41; in Breslau 6, in 85; in Gottingen (up to the year 1919) 12 in women, *i.e.*, in 229 cases, 28 were in women (12.22%) and 201 in men. In 772 cases collected from the literature, Kraus found 188 in women (over 23%) and 584 in men.

Esophageal carcinomas appear mostly in older individuals, rarely before 40, most frequently in the fifties. In 144 cases (Breslau and Basle), 31 occurred in the sixties, 36 before the 50th year, 11 before 40, 10 after 70. The oldest was in a woman of 90 years and 7 months with a very small isolated infiltrate. The youngest was in a 21 year old girl. Heimann saw a carcinoma in a 19 year old girl. The material at Gottingen also shows the highest number in the 5th and 6th decades.

The duration of the disease is usually one year, often less. Inanition, due to lack of ability to ingest food is often sufficient to cause death, but severe complications developing as a result of the relations of the carcinoma to its surroundings (p. 645) may hasten exitus. Above a stenosing carcinoma there is dilatation of the tube and atrophy of the walls; food

stagnates, the mucosa is consequently in a state of chronic catarrh and sometimes is covered with many leucoplakic spots (fig. 283).

**Mode of Growth of Esophageal Carcinomas.**— The neoplasm begins as an infiltration with nests starting from the epithelium and penetrating the wall, between the muscle fibers to the serosa; the wall is thus thickened (fig. 286) and the normal layers are forced apart and crushed, while a white, homogeneous, carcinomatous mass of softer or firmer consistency takes their places. The infiltration is in islands, or nests projecting as nodules, or as annular stenosing growths. The musculature in the infiltrated areas usually shows functional hypertrophy for a time.

FIG. 286. Squamous cell carcinoma (slightly cornifying) with infiltration of the wall of the esophagus. K, carcinoma nests, here and there with pearls (p), occupy the mucosa. Sm, submucosa; g, blood vessel; m, muscularis with inner circular (c) and outer longitudinal layer (l); Tf, tunica fibrosa. (Magnifying lens.)

Ulcerative disintegration is favored by ingested material (fig. 287). In exuberantly growing carcinomas, the base of the ulcer is soft, irregular and lumpy, the margins firm, indurated and thrown up in walls (fig. 287). Disintegration may progress far enough to finally diminish the difficulties of swallowing. In the hard scirrhous forms poor in cells, ulcerative destruction is often but slight, the ulcer base is hard, cicatricial and the margin is hardly distinguishable. The tube is narrow within the site of a circular scirrhus (fig. 283) and at the same time markedly thickened, not only from the infiltration, but from hypertrophy of the muscularis. Sometimes the infiltration extends in the tunica fibrosa or in the submucosa far from the primary growth even to the gastric serosa of the lesser curvature.

**Relations to the Surrounding Parts** (Topograph. Fig. 82, p. 140).—The greatest danger to the vicinity is perforation of the ulcer; according to data from Gottingen, it occurs in 45%. It usually occurs after previous infiltration of the neighboring organs; the growth disintegrates when the ulceration of the main tumor progresses to it. In other cases perforation is direct because the tumor suppurates; mediastinitis and suppurative phlegmons are results. The respiratory organs are in great danger (trachea, bronchi and lungs, especially to the right; fig. 287). In most cases, the carcinomatous material reaching the lungs produces purulent and necrotic bronchopneumonia, rarely tumor implantation, but some-

times the carcinoma does invade the trachea and bronchi. Pleura and pericardium, even the auricles are endangered (fig. 82 left auricle).

Erosion of large blood vessels with profuse fatal hemorrhage is rarer. The author saw this 4 times of the aorta in 126 cases; the perforation may

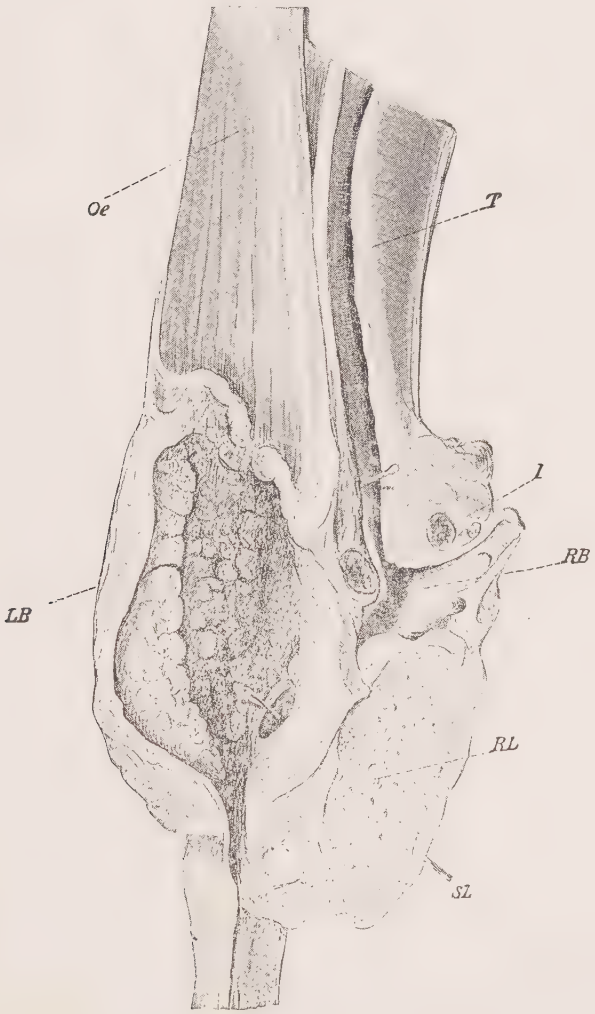



FIG. 287.—Ulcerative, soft, stenosing annular carcinoma of esophagus, at level of bifurcation; rupture into right lung; ulcer of carcinoma with raised margins and nodular base. SL, probe leading from the broad area of perforation into right lung. RB, right bronchus. In l. bronchus (LB) over which the carcinoma is situated, a second probe is introduced leading into the trachea (T); Oe, dilated upper part of esophagus; l, bronchial nodes.

have the shape of a small rounded hole, or a very irregular slit; it has been reported of the pulmonary artery, carotids (fig. 82), inferior thyroid, etc., the latter indirectly from a carcinomatous periesophageal cavity. [For

perforation of the aorta, see also Carr, J. G. and Hanford, C. W., Am. J. Med. Sci., 164: 340: 1922.—*Translator.*]

The lymph nodes of the esophagus (Sakata) drain large areas; the upper third, the deep cervical and peritracheal nodes; the middle third, the bronchial and posterior mediastinal nodes, and the lower third, the posterior mediastinal and upper gastric nodes. The nodes along the esophagus are often involved but seldom sufficiently above, or more frequently, below the tumor, especially at the cardia, to cause esophageal or cardia stenosis (fig. 288). Secondary rupture into the lumen of the esophagus or stomach is rare, (lit. by Borrmann), but the author saw rupture into the trachea with a hole to admit a thumb in the esophagus.

But nevertheless, in some cases the cervical lymph nodes and the connective tissue of the neck show enormous infiltration of importance in diagnosis; this infiltration may obstruct the upper channels and be discernible long before symptoms of esophageal stenosis appear.

Two examples may illustrate: strong man, 50 years old, nodule on the right side of the neck, of four months duration, enlarged rapidly in 6 weeks, an immense tumor, bilateral, extending from the maxillary angle to the clavicle, hoarseness, 8 weeks later death from asphyxia; autopsy: carcinoma of the esophagus in the middle portion, extent 4 cm., no stenosis, several perforations of bronchi, rupture of lymph nodes into both jugulars, no metastases to lungs, but several growths in the peritoneal serosa, compression of both vagi, death from edema of the glottis. A second case is even more interesting, girl of 21 years, death from deglutition pneumonia, left side of the neck seat of a tumor as large as a fist grown tight to the vessels, operation of extirpation with vessels and vagus; microscopically: cornifying carcinoma; at autopsy a primary tumor was found macroscopically hardly recognizable, quite flat, ulcerated, surrounded by a low wall in the upper part of the esophagus, microscopically, typical cornifying carcinoma. This case is also rare on account of the youth of the victim. In another case, 52 year old man, the jugular veins of both sides were varicose, to the thickness of a hen's egg, and filled with red thrombi due to the proximal part being surrounded and infiltrated by carcinomatous lymph nodes (see I. Diss. Struckmeyer).

The frequent involvements of the recurrens are likewise of diagnostic importance since they may be invaded or compressed by the main tumor or metastases on one or both sides. Involvement of a recurrens causes paralysis of the vocal cord on the same side; the hoarseness often appears earlier than the local difficulties in the esophagus. (The recurrent nerves, p. 140, pass on either side of the neck between the trachea and esophagus. They can be found most easily at autopsy, close to the trachea and are then followed downward.)

The esophageal narrowing by aneurysms of the aorta should be remembered in the differential diagnosis. It has happened that a bougie passed for a supposed esophageal carcinoma has perforated an aneurysm of the aorta.

Invasion by continuity to the thoracic vertebrae is very rare but may be accompanied by compression myelitis. The author saw such a case in a 40 year old man without esophageal symptoms; 10 days before death

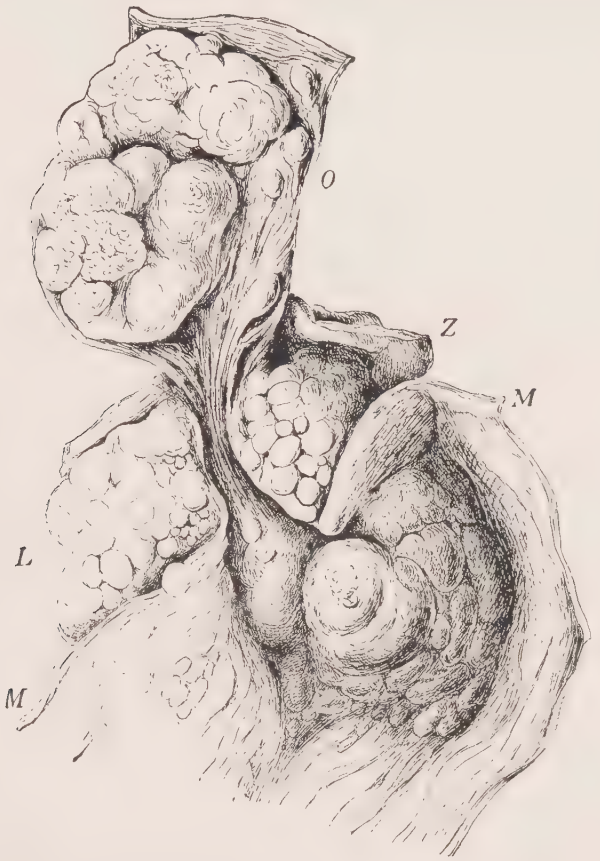



FIG. 288.—Carcinoma of esophagus (O) with immense infiltration of lower lymph nodes (L) those below the diaphragm (Z) and behind the stomach (M) marked bulging, infiltration and superficial ulceration of posterior wall of stomach in woman 57 years old.

a sudden transverse paralysis occurred; the 4th and 5th thoracic vertebrae were completely carcinomatous and had crushed the cord.

The relations are varied between esophageal carcinoma and the stomach. The carcinoma, usually as an ulcer, may continue into the cardia (1), or as an essentially nodular or diffuse infiltration into the gastric mucosa (2), or innumerable (lymphogenous), coin shaped metastases occur in the gastric submucosa, mucosa and muscularis, (3), or

carcinomatous lymph nodes around the cardia cause stenosis (4) and infiltrate the stomach as far as the mucosa (5), which ulcerates and appears like a primary gastric tumor.

Metastases to more distant organs are sometimes absent, but appear in the lungs and liver, according to the material in Basle in 23% and in Gottingen in 18%, mostly in deep seated carcinomas. Occasionally they appear in other places, *e.g.*, the pancreas, kidneys (in Gottingen in 8.2%), in bones, even in the brain (in about 4% of cases), rarely in almost all organs as the author saw in a 52 year old man even in the choroidea and skin. In these latter cases microscopic ruptures into veins can be detected occasionally. With few exceptions, some carcinomatous lymph nodes are found (bronchial, tracheal, epigastric).

Secondary carcinoma of the esophagus occasionally occurs by continuity in carcinoma of the stomach (see p. 694), larynx, thyroid, bronchi and pharynx. Sometimes the growths are interrupted when spread via the lymph route. This causes submucous, isolated, smooth nodules which may appear pedunculated like polyps, etc.

### Disturbances of the Lumen and Continuity

**Stenosis.**—(1) May be congenital (p. 631), (2) due to obstructing factors such as foreign bodies, polyps, carcinoma, oidium, (3) due to changes in the wall such as scars from escharotics, syphilis, other ulcerations, scarlet diphtheria, traumas, phlegmons, tumors, (4) due to compression from surrounding tissue (goiters, tumors, or lymph nodes, lungs pleura, mediastinum, aneurysms of the aorta, subclavian, carotid, etc.); for dysphagia spastica, see below—for dysphagia lusoria, see p. 634.

See the work of Kovacs and Stoerk in reference to dislocations mostly to the right posteriorly, and compression by left auricular cardiac enlargement.

**Dilatation or Ectasia and the Formation of Diverticuli.**—Differentiation is made between general and partial dilatation or ectasia in which the whole esophagus or only a portion is dilated in its whole circumference. If the whole circumference is not dilated, but only a circumscribed part of the wall bulges outward, it is spoken of as a diverticulum. General dilatation, or dilatation of only the lower part, spindle-shaped, diffuse, idiopathic, without organic stenosis is rare, and occurs (1) congenitally as a developmental disturbance (very rare) or acquired, from a nervous disturbance of vagus function, *i.e.*, the tube dilates from primary atony (Netter, Rosenheim), the paralytic form. Hypertrophy of the musculature is absent, or—and this is the general opinion—the dilatation is developed after spasmodic closure of the cardia as cardiospasm (Mikulicz) or cardioparesis (Meltzer). Relaxation of the cardiac opening does not

occur because of disturbance of the vagus. These cases offer the clinical picture of dysphagia spastica or esophagism (Strumpell). Ectasia at times is only slight, but may assume enormous proportions, the esophagus reaching the circumference of a man's arm and accompanied by lengthening, tortuosity and also almost without exception with hypertrophy of the wall (fig. 289).

FIG. 289.—Diffuse (spasmogenic) ectasia and hypertrophy of the lower portion of the esophagus (bottle-shaped), woman, cook, 54 years old, diabetic. Death from food entering bronchi. Esophagus 31 cm. long (normal 25 cm.); inner circumference of ectasia 20 cm.; cardia of normal width (5.5 cm.); thickness of wall in area of ectasia 4 mm. The dilated esophagus contained mashed potatoes. The inner surface partly ulcerated, was covered with oidium albicans. The muscle bundles, partly exfoliated and calcified. ⅓ nat. size. U, uvula: E, epiglottis; St. goiter; A, aorta; C, cardia; M, stomach.

Such an esophagus may hold 1.5 to 2 liters of contents; its normal capacity is 150 cc. or less. Normally 25 cm. long, it may reach 31 cm. (see illustr.) and even 46 cm. with a circumference of 30 cm. If merely the lower part is dilated and the cardia free, it is also spoken of as crop or pre-stomach, possibly congenital (lit. Heinemann).

According to Zaaijer, the dilated portion never reaches below the esophageal hiatus. The abdominal narrow portion is supposed to be especially long (3–4 cm.) and the circular muscle layer of the abominal end must be poorly developed. Gastric ptosis is supposed to favor the development of a neurogenous cardiospasm.

To understand esophagism, or pathological cardia closure, requires some introductory physiological observations.

The cardia receives its innervation from local ganglion cells which maintain contraction of the cardia—the resting stage, closure. Probably impulses from centers in the central nervous system through fibers of the vagus increase this tonus of the cardia musculature. Opening, or relaxation, the active function of the cardia, is normally transmitted to the cardia as an impulse by the vagi through action of the longitudinal musculature, the dilators.

Several possibilities may be considered in pathological functional closure. Some suppose that the relaxing influence of the vagi is absent (as in vagus resection). It is therefore a cardioparalysis. But it is possible that autochthonous processes in the ganglio-muscular apparatus of the cardia itself produce a hypertonic "cardiospasm" which the normal dilating influences are unable to overcome; it might be that the above mentioned central impulses increase the tonus by central stimulation, or by stimulation of the vagus fibers; coincident vagus-pulse, bradycardia, as a sign of vagus irritation, may be present (Kaufmann). According to Kraus, to paralysis is added still another neurogenous loss of tonus of the esophagus, also depending on the vagus, a permanent relaxation or paralysis of a part of the esophageal musculature. This explains the dilatation of vagus paralysis, or after section of these nerves. But the x-rays show that the dilated portion retains its peristaltic activity (Zaaijer). The usually remarkable hypertrophy of the wall of the dilated portion surely indicates an increased function in opposing the increased resistance of the cardia. For discussion of these questions, see Meltzer, Kraus, Zweig, (lit.), Dierling (lit.) Zaaijer, Thieding.

Autopsies discover no other reasons for the dilatation (lit. in appendix). Beneke advises an investigation in situ with due consideration to a possible valve mechanism, *i.e.*, filling the esophagus with water.

In cases of the second group, (2), the wall, especially the circular muscle layer is thickened, and if the usual secondary chronic catarrh is present, it is filled with small cell infiltrates, especially in the submucosa, and fibrous foci and strands.

The inner surface may be practically lined by innumerable, white, slightly raised islands of squamous epithelium as a leucoplakia. In a 58 year old woman, suffering for 7 years, greatly emaciated, weight 50

pounds, the esophagus was dilated, spindle shaped, 2 fingers wide and thick walled. It may be coated with oidium, eroded or deeply ulcerated, and the thickened muscle bundles exfoliated, or undergoing fatty degeneration and calcification (fig. 289).

Degenerative changes have been found in the vagi in a few cases (Kraus,—not verified by others, comp. Harbitz).

In other cases having the symptoms of cardiospasm during life, the autopsy shows but slight degrees of spindle or diffuse dilatation and hypertrophy and both macroscopically and microscopically no changes but

FIG. 290.—Typical traction diverticulum of esophagus. Apex of tent-like diverticulum fixed to anthracotic bronchial lymph nodes (b); t, trachea; nat. size.

chronic catarrh. In such a case observed by the author (72 year old man), the esophagus, open above, was 4 cm.; in the middle 5½ cm.; and at the cardia 3 cm. in circumference; the greatest thickness of the wall was 0.6 cm. It must be mentioned that, corresponding to an older conception, some authors still show a tendency to view local pathological changes of the mucosa as of etiological importance (Kaufmann and Kienbock, etc.), while most workers consider them secondary (lit. by Stierlin). The disease usually begins between the 20th and 40th years, may last for decades and cause death from inanition.

A diffuse stasis ectasia develops orally to strictures, but not in all cases. The dilatation may be cylindrical or spindle-shaped and is usually accompanied by hypertrophy of the circular muscle which gradually decreases ascending from the dilatation (fig. 283).

Dilatation is usually slight since regurgitation occurs (Rosenheim). Several times the author saw a not inconsiderable dilatation below the stricture, doubtless caused by ascending gastric contents. Perhaps in these rare cases, there is atony of the muscle of the cardia leaving it permanently open. The author also saw pronounced leucoplakia in the dilated lower part of the esophagus with a carcinoma at the level of the bifurcation in a laborer 55 years of age.

Diverticuli of the esophagus may be divided, according to Zenker, into traction and pulsion. The former develop by pull from without, the latter, usually in the pharyngeal region, enlarge essentially by pressure from within.

(*a*) **Traction diverticuli of the esophagus** (Zenker), fig. 290, are found not rarely on the anterior or lateral walls, mostly in the middle third near the bifurcation where the bronchial lymph nodes lie against the esophagus, rarely in the upper or lower third. A rounded or elongated plicated opening is seen which leads into a tent-like or funnel-shaped sacculation of the wall, from 0.5 to 1 cm. in depth. The direction of the diverticulum is usually oblique and upwards, rarely in another direction, for instance, horizontal. The apex of the funnel practically always shows cicatricial tissue belonging to an atrophied bronchial lymph node, sometimes a hardly recognizable remnant of one, or a cicatricial cord from a chronic mediastinitis continued in the direction of the trachea, or a bronchus.

The lymph nodes are chiefly simply anthracotic or softened and shrunken, naturally in older individuals; more rarely they are tuberculous (cheesy-chalky-fibrous).

The mucosa of the apex of the diverticulum may also contain transported anthracotic pigment (p. 254). Sometimes the apex is cicatricial from a preceding ulcerating lymph node-esophageal fistula.

According to Rokitansky, a diverticulum is caused by extension of a perilymphadenitis to the esophageal walls and the subsequent cicatricial retraction of the granulation tissue. Sometimes several diverticuli are present.

Klebs suggested that some traction diverticuli depended on fetal anomalies, and Ribbert attempted to show that most traction diverticuli were embryonal disturbances, thinking that incomplete separation of the esophagus and trachea left a persistent cord-like union. A muscular defect resulted where the cord was attached and there the mucosa was everted; the adhesions to inflammatory lymph nodes were secondary.

Even if admitted that traction diverticuli can develop in this way (but as a rule solitary) (Heinen), nevertheless, this interesting theory does not harmonize with the majority of cases which correspond with Zenker's conception; no such cord is present, only direct fixation by scar tissue, and several diverticuli are developed. The same opinion is voiced by Hausmann, Brosch, Bevermann, and especially Riebold. The older conception is also supported by the experience of the Institute of Basle which has given quite careful attention to these diverticuli since the work of Oekonomides.

These diverticuli usually cause no symptoms, but apical perforation from decubitus or foreign bodies produces very grave consequences and therefore they are of practical importance. Chronic or acute suppuration occurs in the vicinity of the esophagus or in the mediastinum, pericardium, bronchi, lungs, even the large vessels, and secondary multiple perforations lead into the pleurae. A fistulous communication between the esophagus and a bronchus allows the aspiration of infected material with gangrene of the lung as a result, (Schlagenhaufer and Starck). Carcinomas have developed in diverticuli (p. 643).

If a traction diverticulum is distended by pressure from within it is spoken of as a traction-pulsion-diverticulum (Oekonomides, Brosch).

(*b*) **Zenker's pulsion diverticuli** (fig. 291) (rare) are saccular or bottle-shaped spaces with narrow or wide openings often flattened slightly antero-posteriorly. The typical pulsion diverticulum occurs constantly in the posterior pharyngeal wall; the entrance is exactly at the border between pharynx and esophagus behind the cricoid cartilage, above the first narrow place (p. 642).

According to Killian, their usual location is 17 cm. from the incisors.

They are also called saccular diverticuli (Huber) or dorsal diverticuli in contradistinction to lateral pharyngeal diverticuli. Starck calls them "pharyngo-esophageal diverticuli;" W. Rosenthal "border diverticuli," or "hypo-pharyngeal diverticuli."

The walls consist chiefly of mucosa and submucosa, the latter thickened. According to some opinions, muscle fibers are absent or present at most in the neck of the diverticulum, so that the submucosa and mucosa escape between the fibers of the inferior pharyngeal constrictor in the fashion of a hernia (pharyngocele). But others found microscopic muscle fibers in the walls and call them pharyngectasia, *i.e.*, sacculation of the whole wall.

According to Starck 75% occur in men; advanced age is the rule.

Typical dorsal diverticuli extend backward between the esophagus and spinal column, varying in size between a cherry and a fist. Sometimes the tumor appears in the neck and enlarges during eating perhaps

sufficiently to compress the esophagus, whereupon any food introduced is at once regurgitated, but the contents of the sac may be emptied between

FIG. 291.—Large pulsion diverticulum of pharynx, lateral view; man 80 years old. The sack (D) 8 cm. long (stuffed with cotton) passes at a, between lowest fibres of inferior pharyngeal constrictor; these fibres continue on the neck of the sack becoming lost on its surface. They cross with fibres b, which, diverging from the esophagus, pass on the diverticulum to be lost on its surface. C, crico-pharyngeal muscle and th, thyro-pharyngeal muscle together forming C inferior constrictor of pharynx; d, sup. cornua of thyroid cartilage; e, greater cornua of hyoid bone; l, sup. laryng. nerve; O, esophagus; T, trachea; M, middle pharyngeal constrictor and parts of the superior; Z, tongue. Mucosa of diverticulum quite smooth, somewhat thickened; thickness of its wall 0.5–0.6 mm.; about ⅔ nat. size.

meals by choking movements. Consequently the patients become much emaciated and finally die of inanition. In some cases clucking and gur-

gling noises can be heard during swallowing and the palpating hand perceives movements. The x-rays are important in the diagnosis (details by Hochenegg). With the sac empty, a probe passed perpendicularly, may glide past it, but if arched and passed along the posterior wall, it enters the sac; this always occurs if the probe is used when the sac is filled. In quite rare cases food (which may remain for weeks) decomposes, causing epithelial maceration, infection by pyogenic organisms, ulceration, and periesophageal phlegmons (Maraguma). For carcinoma, see p. 643.

As to the development of pulsion diverticuli, several opinions are held: according to Zenker, they are pharyngoceles, mucosa hernias, *i.e.*, an out-pouching of submucosa and mucosa, and their development depends on an anatomical predisposition, viz., the thinness and transverse parallel arrangement of the inferior pharyngeal constrictor fibers, *i.e.*, the open angle, formed by the pars fundiformis and the pars obliquata of the cricopharyngeus. The direct cause is supplied by mechanical factors, traumas, in a wider sense such as forcible quick swallowing, jamming of large solid morsels, bad dentition (Kloiber, lit.), increased expiratory air pressure (according to Rosenthal, sneezing, coughing, blowing of musical instruments) forcing the atrophic muscle fibers apart, or tearing them. The searching investigations of Starck support this conception. Others assume there is a pharyngeal ectasia, or out-pouching of the whole wall. This opinion is based on cases in which cross striated muscle fibers were found in the wall of the sac. There is reason to suppose that the fundamental cause of these ectasias, their direct cause being the mechanical lesions given above, consists of some disturbance in the closure of a fetal cleft or remains of an individual internal gill furrow (visceral pouches) (Konig v. Bergmann).

According to Killian's theory, besides individual predisposing factors, food, insufficiently chewed, is capable of disturbing the normal reflex movements which open the esophagus (p. 642; fundiform muscle, *i.e.*, the aboral part of the cricopharyngeal muscle); this spastic annular obstruction holds larger food particles. The diverticulum gradually forms above this in the angle mentioned; this esophageal spasm is thus the counterpart of cardiospasm. If this theory is accepted it must further be assumed that the spasm finally becomes inactive, which, according to the author's experience, probably occurs as shown by diverticuli with very wide necks.

Brosch has described epibronchial pulsion diverticuli situated typically on the anterior and left periphery of the esophagus over the left bronchus. Other pulsion diverticuli which occur remarkably often at the lower end are called "epiphrenal" by Rosenthal; their origin is supposed to be due to traction (Rosenthal) and other mechanical factors as in border diverticuli

(Riebold). In their macroscopic shapes both epibronchial and epiphrenal pulsion diverticuli resemble those of Zenker.

According to Kostanecki, lateral pharyngeal diverticuli represent merely traces of branchial clefts, or incomplete branchial fistulae with secondary dilatation. They are always higher than border diverticuli, never below the pyriform sinus, and are analogous to branchiogenic cyst tumors and fistulae of the neck (p. 328). Starck designates them pharyngeal pulsion diverticuli.

**Foreign Bodies. Perforation of the Esophagus. Fistulae. Rupture**

Small pointed foreign bodies are especially dangerous (bone splinters, plum stones, etc.), and become stuck in the wall; the arrival of bacteria causes periesophageal suppurating phlegmons (mediastinitis). Apart from the consequences of these phlegmons (*i.e.*, suppurative pleuritis, pericarditis, abscesses and gangrene of the lungs, etc.), the foreign body itself penetrating adjacent tissue may, for example, perforate the aorta (lit. by Chiari) or pulmonary artery. Foreign bodies are wedged most frequently at the narrowing at the cricoid cartilage (p. 642) (lit. in ref. to foreign bodies by Vogel). Very pointed thin foreign bodies such as needles, hairs, etc., (Pick) may wander through the wall and be found accidentally during later autopsy in the epicardium, etc. Sometimes foreign bodies become encapsulated and embedded in the tissues.

Large foreign bodies exert pressure on the mucosa (pressure-gangrene); small hard foreign bodies may do likewise (bone fragments). The entrance of foreign bodies into traction diverticuli may have very grave results (p. 653).

See page 638 in reference to the introduction of actinomyces on foreign bodies.

To esophageal perforation little may be added. (1) It may take place from within outward, from foreign bodies (Hacker, lit.) and perforating ulcers (under carcinoma), trauma from bougies (B. Fischer; the case p. 634) and from rare auto-digestion. (2) From without inward, it occurs from aneurysms of the aorta (p. 139), from spondylitis (rare) (Diernfellner); most perforations are caused by lymph nodes, tuberculous or anthracotic, especially those lying around the bifurcation. The former often perforate simultaneously into the esophagus and trachea and cause rapid death or lead to fistulae or cicatrization of fistulae and traction diverticuli, etc. Rupture of suppurating lymph nodes is rare, as for example, after scarlet diphtheria. In a 4 year old boy with necrotic esophagitis, the author saw a perforation as large as a pea of a softened lymph node into the esophagus (4 cm. above the cardia) and into the aorta on the right anterior aspect (admitted a fine probe). Carcinomatous lymph nodes may become fistulous in primary esophageal carcinoma (p.

646) or a gastric carcinoma also, as in a 45 year old woman; they may communicate through a broad crateriform opening. In reference to rare spontaneous ruptures (longitudinal tears, usually in the lower part of the esophagus), see Borsch, lit. See Zuppinger in reference to non-traumatic perforations in childhood. According to Petren, rupture may occur purely from the trauma of sudden increase in pressure (over-distension, forcible vomiting), without previous changes in the esophagus, as also demonstrated anatomically by Beneke. This is quickly followed by mediastinal and subcutaneous emphysema, pneumothorax, exudative pleuritis, mediastinal phlegmons, peritonitis. Death occurs usually in 24 hours but the author saw patients live for several days.

### Parasites

Oidium albicans is important and frequent (p. 561), usually in coatings over the epithelial layer, white, or, if sporulating, yellow, acid, sticky and loosely attached as the so-called thrush membranes (mistaken for desquamated epithelium). The coating is striped, or diffuse, sometimes massive enough to form thick poultaceous lumps, filling the lumen. The fungi rarely penetrate deeply into the wall.

Thrush of the esophagus is usually combined with thrush of the uppermost parts of the digestive tract; the membranes may reach to the cardia but rarely into the stomach, where it may spread deep into the mucosa (Maresch), but more likely, ignoring the stomach, it progresses to the duodenum.

## STOMACH

**Anatomy.**—The stomach wall consists of 6 layers: (*a*) mucosa with glands and small indentations or depressions on the surface; (*b*) muscularis mucosae; (*c*) submucosa; (*d*) muscularis (inner circular—outer longitudinal); (*e*) subserosa; (*f*) serosa (peritoneum). The mucosa is covered with a simple layer of mucus-producing cylindrical cell epithelium, goblet cells when the contents are gone (for the histology of the surface epithelium, see Heiderick). Glands are abundant as simple or forked blind tubes lined with cylindrical epithelium resting on a basement membrane of flat cells. One or more ducts empty into the small depressions (so-called neck) on the surface. The glands in the pylorus are further apart as a rule. They are divided into: fundus glands, about 100 to 1 sq. mm., occupying the body and fundus, and (2) pyloric glands; the latter have only one kind of cells while fundus glands have two; *i.e.*, besides the cylindrical main cells there are larger, angular, numerically few, parietal cells in the rows of chief cells pushed against the periphery; they stain intensively with anilin dyes. The parietal cells are said to supply hydrochloric acid (Heid-

enhain), the chief cells the pepsin of the gastric juice. The pyloric glands are situated only in a small zone of the pylorus and have much longer ducts than the fundus glands; the interposed islands of mucosa are called "villi." The pyloric portion supplies an alkaline secretion, parietal cells are absent. The mucosa is rich in end arteries which arise at the mucosa near the surface and form a capillary network emptying into the veins (interesting details by Disse). Larger arteries course between serosa and muscularis and send twigs to the submucosa in an oblique direction (details by Disse, Jatrou, lit. Hofmann and Nather), from which branching end arteries pass into the mucosa to change into capillaries near the surface. Lymph follicles occur in varying numbers and sizes; most of them are in the pyloric part of the mucosa. There are lymph vessels in the mucosa, submucosa and in the intermuscular and subperitoneal tissues; the submucous network is especially wide (Cuneo).

When the stomach contracts, the mucosa folds into coarse, convoluted, longitudinal plications with small circular, or angular circumscribed areas smoothed out from the pulling.

In reference to the inconstancy of its shape and position under normal and pathological conditions, see His, C. Hasse, Strecker and Ponfick, (Topograph, Atlas der mediz. chirurg. Diagnostik, Jena, G. Fischer), Simmonds, Wernstedt, Beckey, W. Thoma, Aschoff; Forssell distinguishes 4 divisions: fundus, body (chief portion), pyloric antrum and pyloric opening; between the body and the antrum the isthmus is like a narrow tubular connection, the so-called physiological pseudo-hour-glass stomach. Several longitudinal folds appear on the lesser curvature, forming the so-called gastric path (Stieve, Elze, and cf. Volkmann, Westphal).

Gastric rigor mortis (Mangold, Hecht) may fix vital contractions.

### Post Mortem Changes of the Stomach

These must be taken into consideration more than in any other organ in judging pathological findings.

**Hypostasis.**- Settling of blood in dependent portions (fundus) causes dark red blotching composed of numerous vessels (veins) and diffused blood pigment. They must not be mistaken for hemorrhages.

Acid Softening. Acid gastromalacia is due to autodigestion if sufficient pepsin and HCl are present, or if the stomach contains acid pathological decomposition products. This condition begins much earlier than true post mortem decomposition. Slight activity of the gastric juice is manifested by cloudiness and maceration of the cylindrical epithelium and the squamous epithelium at the transition into the esophagus. In gastromalacia, swelling occurs first and is succeeded by softening but only of those portions which lie below the level of fluid, for that reason especially

the fundus. It is often very pronounced in small children, whose stomachs were filled with milk; the acid fermentation of the milk contributes to the stomach becoming gelatinous and pale.

The mucosa is soft and can be stripped off; if it contains little blood it is white, if vascular, it is brown, and pultaceous, often only in spots. The brown color is caused by blood pigment altered in the acid gastric juice. Submucosa and muscularis may then soften and disappear; the wall becomes translucent; friable, ragged holes appear with liquefying margins. The softening sometimes extends to the vicinity and digestion may remove the cells and leave a delicate fibrous network in the spleen, liver, through the diaphragm, even into the lungs, pericardium, etc. Gastric juice often enters the esophagus first and dissolves it, or from here it enters the respiratory channels and digests large cavities in the lungs (for instance, during transportation of the body, p. 358) which then contain an acid fluid which distinguishes them from gangrenous foci which appear similar but show an alkaline reaction. It also frequently causes an emphysematous appearance in the lungs.

According to the investigations of Bamberger, intravital autodigestion does not take place in a stomach previously unchanged, hence if it appears there must be disturbances of circulation such as thrombosis of the celiac— and sup. mesenteric arteries, etc. Such circumscribed areas, vulnerable to the gastric juice, look like round ulcers (p. 677).

Post mortem emphysema of the stomach develops chiefly in the loose submucosa from bacteria which penetrate the mucosa or produce gas in blood vessels. The blistered, lumpy gastric wall crackles when handled. There occur a few cases of intravital interstitial gastric emphysema caused by gas forming organisms, but they are better known in the bowel (p. 767) (Orlandi; intestinal pneumatoma, illustr.; Dupraz experimental lit.; Hahn, intestinal cystoid pneumatosis in man; see emphysema of urinary bladder and vagina).

Post Mortem Discoloration of the Mucosa. Not rarely, especially in venous congestion and chronic gastric catarrh, the sulphuretted hydrogen of decomposition produces a dark green to black discoloration of the mucosa (pseudomelanosis). According to E. Neumann, however, pseudomelanin is not simply caused by decomposition processes but iron-containing pigment (hemosiderin) was deposited during life from the disintegration of hemoglobin. This pigment turns to black iron sulphid in the presence of sulphuretted hydrogen. Pseudomelanosis disappears on the application of diluted HCl; true melanin in the epidermis and cutis, in the retina and choroid in melanotic tumors, etc., contains no iron but sulphur and nitrogen, and is a product of the complicated disintegration of protein substances, very different from blood pigment. In interpreting

the macroscopic appearance of the gastric (and intestinal) mucosa, great care must be used on account of the changing contraction, digestive phases, post mortem changes, and mechanical lesions (Tugendreich).

### Congenital Anomalies

Agastria, absence, and microgastria, congenital smallness of the stomach, are rare.

Hour glass stomach may be simulated by abnormal contraction of the musculature between the cardia and pylorus, also by pyloric contraction in the presence of a dilated upper duodenum from a stenosis below. True congenital hour glass stomach has never been observed (Heigel, lit.); for acquired hour glass stomach, see p. 687 and 707. Nauwerk recently renewed attention to congenital gastric diverticuli which contain an accessory pancreas at their bases as a cause (Handtmann, lit.; Conjetzney). The author saw such pancreatic diverticuli in the duodenum. For acquired diverticuli, see p. 716. Connatal atresia of the cardia or pylorus is usually combined with other malformations.

Congenital pyloric stenosis is divided into two main types: (1) the congenital narrowness of the mucous tube in the pyloric portion, described by Landerer and Maier, which may be combined with congenital hypertrophy of the muscularis. They occur almost exclusively in adults. Their occurrence is questioned (Meinel), but according to Chiari (lit.), who supports Maylard, they are definite entities. Maier's cases (adults) showed no muscle hypertrophy, nor did Schafer's case (10 months old boy). Krompecher believes combined cases are sclerostenoses (p. 668). (2) Stenoses from pure muscular thickening are the hypertrophic pyloric stenoses of sucklings (Hirschsprung). The pylorus becomes a tube 2 to 3 cm. long as thick as a little finger, straight or slightly bent, cicatricial in hardness and projecting into the duodenum. The hypertrophy is due to increase in mass of the individual fibers (Tanaka); the other layers show no histological changes. The mucosa is folded longitudinally and thus secondarily narrows the lumen. The genesis is under dispute; it may be an original anomaly of architecture, a sort of tumor-like muscle hyperplasia (Hirschsprung), or an effect of spasm (Thomson) from functional disturbance of the nerves coordinating the muscular movements of the stomach and pylorus, creating an antagonism even in utero (ingestion of amniotic fluid), with increased labor, and thus "functional hypertrophy" of the pyloric musculature. This assumption of pylorospasm (Pfaundler, Langemak) with a congenital background and subsequent work hypertrophy of the pylorus (Wernstedt) is shared by many. Others assume that spasm caused perhaps by anomalous secretion produces the primary hypertrophy (Hertz). Thickenings of the mucosa (Arregger)

or mucous adenomyomas (Magnus-Alsleben) as causes of stenosis are exceptions. Some children perish of inanition, others recover, for the stenosis disappears in a certain number of cases. Isolated individuals (Chiari) retain the stenosis into adult life (Koch). Various operations are often curative (lit. in appendix).

In situs sagittalis the original perpendicular position is maintained.

Ectopy of the stomach into the left pleural cavity has been observed in diaphragmatic hernias (see there); the stomach may appear in umbilical hernias (see there).

Transposition of the stomach (duodenum and spleen) was observed by the author in a case described by Halff (lit.) (Lochte, Oberndorfer).

### Circulatory Disturbances

**Anemia.**—In general anemia, the mucosa is white, in chronic anemia, it is also atrophic (thin).

**Hyperemia.**—Active hyperemia is due to irritation from various ingesta, *e.g.*, alcohol, and precedes any acute inflammation. The mucosa is a rosy color. Acute congestion is often very difficult to demonstrate at autopsy; it is most frequent in the pyloric portion as a diffuse or spotted redness.

Passive hyperemia is very frequent due to congestion in the portal vein as in cirrhosis of the liver, or to the general congestion of cardiac and pulmonary diseases. The mucosa is blue violet or, in the presence of acid stomach contents, brown, spotted; dark brown to black gray discolorations (pseudomelanosis, p. 659) are due to hemorrhages. The submucosa may be edematous, making the wall appear thickened.

**Hemorrhages.**—Small hemorrhages in the mucosa are due most frequently to congestion as in cardiac disease, cirrhosis of the liver, emphysema and frequent vomiting (as in peritonitis).

It must be remembered that the numerous small mucosa veins have but very few anastomoses, and for this reason strong, continuous (spasmodic) contraction of the muscularis will produce intense venous congestion in the mucosa, especially at the apices of its folds. Virchow pointed this out and emphasized that congestion of the gastric mucosa is produced by disturbances of the circulation of blood in the portal vein and its branches and may cause hemorrhagic necroses and erosions. Hagemann thinks that punctate hemorrhages might be caused by a rebound of blood when sudden increases of blood pressure occur in the portal system.

Hemorrhages are often an agonal phenomenon. In the mucosa they may be small, punctate, multiple, or innumerable, rounded, spotted or striate, corresponding to the apices of the folds of the contracted stom-

ach. Punctate hemorrhages favor the fundus and cardia. The areas, red, brown or almost black in color, become necrotic and appear like stiff flat infarcts; the tissues are digested by the gastric juice which results in the so-called hemorrhagic erosions. These are edged, more or less shallow; their bases may be blood red brown, dark red brown to black (gastric juice), or if the sanguinous material is completely digested, they are pale.

Occasionally the erosions can be seen through the translucent serosa as brown, sharply demarkated, elongated or rounded spots.

There is always a hemorrhage into the gastric cavity, however slight. Occasionally erosions are diffuse and deep, or as deep longitudinal striae almost 1 cm. in width. At times, confluence produces a very irregular map-like design resembling corrosions in their deep red brown to black

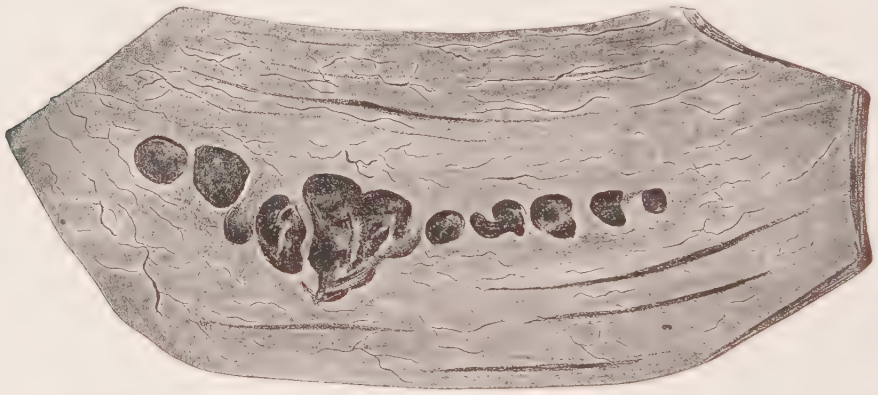


FIG. 292.—Large deep hemorrhagic erosion of stomach arranged in direction of passage of food (near small curvature), all ready to become ulcers. Man 58 with pyloric stenosis; 5/6 nat. size.

color and arrangement. Such erosions may cause severe and even fatal hemorrhages but the same occurs from multiple small erosions (Engelsmann, lit.). For erosions and ulcers after abdominal trauma, see Rossle (lit.).

Small parenchymatous hemorrhages occur in the hemorrhagic diatheses, in severe infectious diseases, *e.g.*, typhoid, pneumonia, spotted fever, and in various poisonings autogenous as in uremia or cholemia, or exogenous such as phosphorus, arsenic, sublimate, acids, alkalies. These hemorrhages are rarely large but have been fatal (Ewald). For fatal parenchymatous hemorrhages of unknown origin, see Fritzsche (lit.).

Small arterial and capillary hemorrhages occur from multiple embolism observed in endocarditis, pneumococcemia (Dieulafoy), etc.; in pronounced cases the gastric mucosa is thickly strewn with punctate hemor-

rhages, or brown erosions or ulcerations derived from them. In such a case (43 year old man with streptococcic necrosis of the pharynx) the author saw the mucosa of the stomach dark red, covered with miliary and submiliary gray dots which were necroses with hyalin thrombi and streptococci. W. H. Schultze found the gas bacillus in an artery of an ulcer base in a case of post operative ulceration with vomiting of blood.

But endocarditis sometimes causes embolic occlusions of arterial twigs with subsequent necrosis and deeper ulcers like round ulcers (p. 677).

Beneke uses the word "stigmata" to designate wedge-shaped necroses with or without hemorrhage caused by irritation of gastric nerves and subsequent reflex ischemia sufficient to allow of digestive ulceration; cf. experiments by Kobayashi, Schmincke and critique by Marchand.

Schiff, Ebstein, v. Preuschen demonstrated experimentally that injuries to the central nervous system (anterior corpora quadrigemina, medulla oblongata, upper spinal cord) would initiate bleeding from the gastric mucosa (see under lungs p. 378), and Beneke also found his "stigmata" (see above) in diseases of the central nervous system (meningitis, brain tumor—see Rossle). Gastric hemorrhages, even dangerous, may appear in hysteria or as vicarious menstruation or during ordinary menstruation (Ewald; Marchand).

True melena neonatorum is the name of a symptom complex-hematemesis and bloody diarrheas—caused by gastric and duodenal hemorrhages and very rarely esophageal, (lit. by Meyer, Vorphal) accompanied by erosions and ulcerations appearing during the first days or weeks of life and sometimes ending fatally. According to v. Preuschen, they are due to brain lesions occurring during birth, *i.e.*, irritation of the vasomotor center causing increase of blood pressure and rupture of vessels, (cf. p. 378), but according to Landau, they are embolic occlusions presumably from a thrombus in the umbilical vein passing through the vena cava, the right heart, Botalli's duct, the aorta, into a gastric vein. v. Franque, however, calls attention to a much simpler route of retrograde venous embolism due to the spasmodic respiratory movements and crying, *i.e.*, from the umbilical vein, the short communicating channel into the portal vein to the gastro-intestinal veins (E. Wolff for experiments and lit.). On the other hand, v. Rundstedt thinks of a combination of venous hyperemia readily produced by the change in respiration and circulatory distribution of blood after birth thus causing mucosa hemorrhages, and a reflex ischemia from irritation to nervous centers of the shock accompanying delivery; there is necrosis and subsequent corrosion by the gastric juice. The opinion of Baisch that it is probably an infection is not supported by others for most cases (Vassmer, v. Rundstedt, etc.). Intestinal hemorrhages in the newborn with the symptom of melenia may, among

other things, also be induced by intussusception, and very rarely by volvulus (F. Wolff, Nurnberger).

Post operative, even fatal, gastric and intestinal hemorrhages are of great clinical interest; they occur occasionally after operative procedures anywhere in the body but chiefly in the abdomen (ligation of vessels of the omentum) (v. Eiselsberg). They are caused by direct or retrograde thrombosis in the arterial and venous systems, probably from infection. The hemorrhages (hematemesis) appear once or repeatedly, usually during the first week, and hemorrhages, erosions or ulcerations are found in the gastric mucosa (lit. by Busse and v. Franque, Disse). Similar changes appear in appendicitis from retrograde embolism originating in the veins of the omentum, appendix, meso-appendix (Payr). Payr has produced experimental hemorrhages, erosions and ulcers in the stomach by retrograde embolism in the portal system, (see criticism of these experiments by Yatsushiro). But Beneke, on the other hand, thinks of reflex ischemia produced by irritation of certain nerves; even without primary hemorrhage this creates the vulnerable spot for the action of the gastric juice (p. 662).

More massive hemorrhages appear occasionally, as mentioned, from erosions and the hemorrhagic diatheses (cholemia, etc.). But the excessive venous congestion in disturbances of the portal system (cirrhosis of the liver, pyelo-thrombosis) or cardiac lesions may increase to an hemorrhagic infiltration and occasion considerable, even fatal, hemorrhages. In this type of case the stomach is markedly dilated and filled with a brown black, intimate mixture of blood and gastric contents, or a stiff, gelatinous blood clot, and it is astonishing that a large rupture of some vessel cannot be found at first; the hemorrhage is designated as "parenchymatous." But if the portal vein is injected, rupture of a varix of a gastric vein may perhaps be found, at least, obstruction of the portal system may be demonstrated.

The collection at Basle contains a rare preparation of a submucous varix the size of a bean causing a gastric perforation 2 mm. in size situated on the posterior wall, 3 cm. below the cardia on the lesser curvature. The 19 year old boy died of hematemesis and had a lobulated liver and cicatricial peripyelophlebitis, (spleen 842 gms.). The varix involved the left superior coronary vein. Saxer and Heller also report the rupture of a varix with occlusion of the portal vein (see under liver).

Ulcerative changes (simple ulcer, carcinoma, sarcoma) may open arteries and veins with larger to fatal hemorrhages, but hemorrhages are rarely due to aneurysms of the gastric arteries.

**Changes in the Blood Poured into the Stomach (and Bowel).**—Small quantities of blood are quickly changed by the gastric juice into a fluid

resembling coffee grounds, or into an inky black, or gray fluid streaking the mucus covering the mucosa. More massive hemorrhages, as for example, 1½ liters (in perforation of the aorta by a carcinoma of the esophagus, premonitory smaller hemorrhages previously caused hematemesis of 1½ liters), may make eating and digestion difficult.

In the small intestine through which the blood passes very quickly, only a little fluid blood is found, or foamy red masses, while in the colon the disintegrated blood is thickened to a brown red smeary mass like plum jam or tar in appearance.

### Inflammations

(Cloudy Swelling and Fatty Degeneration, see p. 712.)

**Acute and Chronic Catarrh.**—Acute catarrh of the stomach may be independent, *e.g.*, from dietary errors, too cold or too hot food, overeating, alcohol, etc., or it may accompany other conditions, especially the infectious diseases. The mucosa is swollen, red, and covered with firmly attached, glassy mucus. The epithelial cells and the gland lumena are filled with mucus. The pyloric portion is more extensively involved. Slight catarrh is practically unrecognizable in the cadaver.

**Chronic catarrh** may follow acute catarrh or develop insidiously. It is especially frequent in drinkers, in circulatory disturbances (cirrhosis of the liver, cardiac lesions), when it is called "congestive catarrh," and with ulcers and carcinoma. Likewise the pyloric portion is chiefly or exclusively affected. It is not confined to the gastric surface like acute catarrh, but is shown in all layers. The essential anatomical changes consist of (1) tissue production (hypertrophic catarrh) followed by atrophy, or atrophy of the glands from the beginning. The mucosa of hypertrophic catarrh is coated by thick tenaceous mucus, gray white in color with an admixture of exfoliated epithelium (mostly post mortem) and leucocytes; in the presence of congestion, it is dark red, violet, or brown to slate gray. The latter color is due to changed blood pigment derived from minute extravasations. The mucosa is furthermore somewhat indurated and thickened, the latter slight but sufficient to produce circumscribed, warty and blotchy elevations surrounded by shallow furrows. This is called "verrucose catarrh" or etat mamelonne (fig. 293). The bosses cannot be smoothed out by stretching and thus are differentiated from the small bosses and elevations, the so-called chagrin, in the contracted normal stomach; the verrucae are also larger, broader and higher than the normal elevations (p. 658).

A flat granular mucosa, frequent in status lymphaticus, a nodular hypertrophy or hyperplasia, the counterpart of so-called nodular enteritis,

is due to numerous and enlarged lymph follicles and must not be mistaken for the inflammatory etat mamelonne.

The glands sometimes contribute to the thickening of the mucosa by hypertrophy of their cells, by producing much mucus and by actual ectasia; still the essential factor is the proliferation of interstitial, interglandular connective tissue and in the early stages the infiltration of round cells, especially in the upper layers, even reaching to the surface and into the glands. There are hyperemia, vascular dilatation, and extravasation of red blood cells. Usually the surface epithelium undergoes mucoid degeneration (A. Schmidt). In its further course, the interstitial character is more and more marked, the increase of connective tissue is apparent everywhere. Plasma cells and Russell's bodies are numerous (hyalin globules and granules consisting of cell debris, staining well with carbol fuchsin); the rudimentary lymph follicles are also considerably enlarged and increased in number. The thickened submucosa is firmly attached to the muscularis and the mucosa ceases to be movable. In many cases the muscularis is also thickened and penetrated by broad strands of connective tissue, the serosa is thickened, cloudy and shows fine wrinkles.

In the chronic gastritis of older individuals, a heterotopic gland proliferation is noticed, *i.e.*, glands growing from the mucosa between the fiber bundles of the muscularis mucosae and into the submucosa which is loosened by the inflammatory processes (Nauwerck, Lubarsch, Hallas, Preusse, etc.). It is impossible to differentiate these sharply from the atypical epithelial proliferations (Friedlander) long known in chronic inflammatory conditions of other parts such as the breast, salivary glands and first described by Hauser in gastric ulcers (p. 687). But atypical epithelial proliferations may be heterotopic or not. The designation "atypical" expresses the change in morphological character, and since it may be more or less far reaching, it is difficult or even impossible to decide if it is beginning carcinoma or not (Borst). But usually heterotopic, atypical, glandular proliferations differ from carcinoma; tumor may be suspected because of downward penetration by the more marked atypicalness of the cells of carcinoma, more dense penetration and destruction of a usually circumscribed area, more irregular formation and closer proximity of gland imitations. Since clinical experience shows that chronic gastritis often precedes carcinoma, each case must be carefully judged on its own merits (Hallas). Like Lubarsch, the author is of the opinion that heterotopic atypical gland proliferation may turn into carcinoma, but Borst doubts it. Compare heterotopic atypical gland proliferations in the gall bladder and uterus, in older individuals, in chronic inflammations, in the intestines, where perhaps also developmental disturbances may lead to such glandular displacements.

At times there are circumscribed, more active, proliferations of mucosa and submucosa resulting in polypoid elevations (polypoid gastritis or proliferating gastritis), or thick, button-shaped growths with broad bases, thin stems and usually grouped most thickly in the pyloric portion. Since the active proliferation includes the glandular epithelium, these "polyps" are on the border line of tumors (polypoid adenomas). While in these cases the polyps are doubtless due to chronic inflammation (Meulengracht), in other cases similar polyps may be due to developmental faults of the mucosa (Verse, Ribbert and p. 690). Sometimes only the gastric villi between gland openings are enlarged, sufficiently so, however, to occlude ducts and lead to cystic dilatation of the glands.

A true cystic gastritis is rare (analogous to cystic colitis); in a 45 year old woman after removal of tenaceous mucus, the author saw the inner surface of the smooth, thin-walled stomach covered with innumerable, gray cysts, closely placed, minute, dew drop-like, transparent, somewhat resembling miliary tubercles, and on puncture disclosing viscid mucus. Microscopically, the mucus is retained in individual cysts, because of periglandular productive inflammation and increased (inflammatory) secretion.

Thickening of the wall is particularly marked in the pyloric portion to which the chronic catarrh is quite often confined; it may measure 2 cm., and the connective tissue is added to by functional hypertrophy of the muscularis. Contraction of the connective tissue might produce pyloric stenosis (so-called "benign") (E. Koch and Konjetzny) followed secondarily by gastric ectasia. The pylorus may seem to be the site of a scirrhous carcinoma, especially if the mucosa is contracted and closely attached to the muscularis, and white tendinous strands pass through the muscularis to the serosa which is also thickened, furrowed and wrinkled. In fact the carcinoma may be there, as Hauser, Tilger and Meinel have emphasized, and the microscope may show the scirrhous tumor, poor in cells, hidden under this picture. Conversely, the macroscopic diagnosis of stenosing mucoid carcinoma may be made when the muscularis is merely hypertrophic surrounding the pylorus and undergoing glassy (hyalin) transformation, with a light yellow color. Krompecher (lit.) calls benign pyloric stenosis, "sclero-stenosis;" see under "linitis plastica" and contracted stomach, p. 668. In reference to chronic duodenal ulcers as causes of "benign pyloric stenosis," see Clairmont.

Glandular atrophy, fibrous transformation, smoothing and thinning of the mucosa with preservation of the epithelium, although mucoid, is called atrophic catarrh. (2) It may be (*a*) the final stage of an interstitial gastritis with earlier thickening of the mucosa and final hardness and grayness, while the other layers are permanently thickened by inter-

stitial proliferation. But this is not the rule; rather the glands atrophy primarily (*b*), their epithelium undergoes cloudy swelling and fatty degeneration, the mucosa is pale, opaque and yellow, very thin, and finally unrecognizable macroscopically, as it becomes transformed into a serosa-like, smooth, thin, connective tissue layer with faint traces of glands undergoing fatty degeneration. Since Virchow's description, this change has been called "parenchymatous gastritis." Since normal function is impossible (secretion and absorption), primary atrophic gastritis is followed by stagnation of contents and ectasia.

For the changes in the gastric mucosa in pernicious anemia, see Herzberg (lit.). Attempts at regeneration lead to changes in glandular structure. The atrophy is not the consequence of primary inflammation, but is due rather to the same noxae which cause the inflammatory proliferation of the interstitial tissue. Gastric changes and pernicious anemia are quite probably caused by the same factor (p. 713) with added inflammatory hypertrophy of the pylorus (Kleemann, Mayda).

The fibrous tissue in the whole gastric wall occasionally contracts sufficiently to diminish the total volume of the thick-walled stomach (cirrhotic atrophy, gastric cirrhosis), whereupon it resembles certain forms of scirrhous carcinoma (fig. 317), and the diagnosis must be left to the microscope. Contracted stomach may be divided into total and partial (confined to the pyloric portion).

Such totally contracted stomachs with walls thickened and filled with fibrous tissue with secondary hypertrophy of the muscularis and pearly glistening hyalin fibrous serosae are seen sometimes combined with general fibro-hyperplastic (zuckerguss) peritonitis. The author autopsied such a case (pub. by Sury, lit.) in which the brawny edematous wall was 2 cm. thick, and the pleura and pericardium were covered with "icing" (polyserositis); this serositis, called, among other names, "plastic linitis" (Brinton), was due to chronic venous congestion. Krompecher calls the process "sclerostenosis", and interprets the parietal thickening as the effect of chronic venous congestion with edema and subsequent fibrous induration; the muscular hypertrophy is due to work. Inflammatory irritation from ingested foreign substances often adds to the indurative process. The author and others have pointed out that contracted stomachs may follow phlegmons (p. 669). Plastic linitis frequently masks a small cell carcinoma with especial connective tissue reaction (Krompecher and Makai; see under carcinoma, p. 703). Konjetzny discusses the possibility that plastic linitis may at times be a sequel of healed, or almost healed fibrous carcinoma. Some authors, especially the French, among others Curtis, who first believed in the inflammatory theory (other lit. in appendix), class linitis with carcinoma,

but this must not be accepted for partial sclerosis of the stomach localized to the pyloric region, since Nauwerck, Krompecher, Konjetzny and others have demonstrated the occurrence of entirely benign hypertrophic stenoses. Later investigations seem to show, however, that totally contracted stomachs, as a rule, are carcinomatous (Konjetzny), but this does not discard the possibility of a plastic linitis or simple cirrhosis of the stomach.

**Pseudomembranous Gastritis (fibrinous and diphtheritic).**—This is rare, apart from membranous inflammations due to escharotics. The folds of the hyperemic, swollen mucosa are covered with brown membranes resembling escharotic scabs. Deep, necrotizing (diphtheritic) scabs destroy the mucosa and leave ulcers. Perigastritis may result.

Pseudomembranous gastritis is rare but occurs especially in enfeebled children after swallowing diphtheritic pharyngeal membranes. Rarely, a necrotizing inflammation appears in severe infectious diseases such as small pox, pyemia, typhoid fever, ulcerative endocarditis, puerperal fever, etc. For necrotic processes in scarlet fever, see p. 636.

Purulent gastritis (circumscribed abscess forming, and diffuse phlegmonous), as a primary condition, is rare. The author saw it in drinkers; in a 43 year old man, the phlegmon was confined to the cardia and was followed by peritonitis; streptococci were found. Every loss of substance of the mucosa permits pyogenic organisms to enter the submucosa.

Innumerable pinhead metastatic abscesses like elevations in the mucosa strewn with hemorrhagic spots, emptying a droplet of pus on puncture, were seen by the author in pyemia following an osteomyelitis and abscess in the soft tissues of the upper thigh in a man 22 years of age. Similar foci were found in the mucosa of the intestines and urinary bladder.

Suppurative infiltration and suppurative liquefaction (abscess) of the submucosa undermine the swollen, juicy mucosa, lift it upward like a cushion or boil, and perforate it by rounded holes; if circumscribed suppuration of the wall extends to the musculature, the abscess may perforate the serosa. In true phlegmons, the submucosa remains the chief localization of diffuse, purulent or fibrinopurulent inflammations, but abscess formation may also take place. Should the condition progress to the serosa, peritonitis is the result. The mucosa may show hemorrhages, erosions, necroses and branny fibrin deposits. The gastric wall may be 1 to 1.5 cm. thick. Ackermann saw pyelophlebitic abscesses of the liver as a complication.

Phlegmons may accompany an ulcerating carcinoma, more rarely a simple ulcer or eschars, and have been observed in severe pyemic infections. In a man 50 years old with suppurating carcinoma of the pylorus,

the author saw a gastro-enterostomy followed by phlegmon of the whole stomach and the loop of bowel; the submucosa was moist, yellow white and 1 cm. thick; the mucosa was hemorrhagic and coated with fibrin. Cultures showed streptococci. This extended to the lowest part of the esophagus which was dilated, and to the peritoneum where it ended in fibrino-purulent peritonitis (this case and others in I. Diss. Schnarrwyler, lit.).

After perforation through the mucosa, an abscess may heal with scar formation. Even a diffuse phlegmon may heal in rare cases leaving a contracted stomach with a much thickened, cicatricial submucosa, a musculature traversed by strands of connective tissue and a milky, cloudy, thickened serosa. This opinion of the author is shared by K. Koch (older lit. by Konjetzny). F. Koenig cured some cases by gastric resection. A circumscribed phlegmon may suggest a tumor (v. Stapelmohr) (lit. in appendix).

(Phlegmon of the duodenum is rare; lit. by Ungermann.)

### Specific Infections

Anthrax sometimes causes carbuncular, blood red, nodular, bossed swellings, or numerous, small, bloody infiltrations with edematous surroundings in the mucosa and submucosa. The centers soon become necrotic (like carbuncles). Anthrax bacilli are found in the nodules and their immediate vicinity. These and their spores reach the stomach wall primarily (lit. in reference to this disputed question by Stein, Rochs, v. Baumgarten) with food contaminated with spores (probably seldom in meat infected with anthrax) or secondarily (hematogenous) from a portal of entry anywhere on the body, as for example, the hand.

Tuberculosis of the gastric mucosa is rare; it takes the form of small, sometimes multiple, irregular, "devoured" ulcers, rarely large (as a dessert plate), with cracked, torn, undermined margins sometimes thickened by nodules, and caseous or granular bases; the pyloric region is favored. It usually accompanies intestinal tuberculosis. The rarity of gastric tuberculosis is remarkable since innumerable tubercle bacilli must reach the stomach in ulcerative pulmonary phthisis; they certainly produce intestinal infection frequently enough. It is thought that the acid gastric juice prevents implantation into the gastric mucosa because, although not destructive, it is inhibitory to bacillary growth. But it has been demonstrated (Curschmann, etc.) that a large percentage of phthisics show reduced or absent hydrochloric acid but are, nevertheless, almost immune to gastric tuberculosis. Consequently the importance of HCl or gastric juice in relation to immunity of the gastric mucosa must not be overrated. Also the fact of a small number of follicles in

the gastric mucosa does not supply a satisfactory solution, even if follicular hyperplasia (p. 665) sometimes observed in the gastric mucosa of phthisics, may favor infection. There must be a diminished susceptibility, as shown in animals, or a non-responsivity of the gastric mucosa; furthermore, if the motor activity is unchanged, the constant movement of the ingested material does not permit quiet invasion of tubercle bacilli. Erosions (Marfan, Stelter), minute lesions (animal experiments of Orth), corrosions (Breus) might favor direct infection (Przewoski). Others assume a hematogenous origin (supported by animal experiments) from tuberculous endarteritis (Arloing), or presuppose retrograde or direct infection of the gastric wall by way of the lymphatics from retrogastric lymph nodes (Rosset, Fujii, lit.). Finally direct rupture of regional caseous lymph nodes into the stomach has also been observed (Chiari, Gossmann, Keller).

The most common findings are simple, multiple ulcers, usually in individuals with severe pulmonary and intestinal tuberculosis. It is unusual to find small multiple polypoid excrescences on the sclerotic overhanging margins and bases of older tuberculous ulcers similar to the tumor-like stenosing cecal tuberculosis, but the author saw it occur in a large confluent ulcer, an inch across, located on the posterior gastric wall of the cardia in a phthisical woman 41 years old; also in a single ulcer in the pyloric region of a 15 year old boy. Such cases are transitions into hypertrophic tumor-like tuberculosis (mistaken for carcinoma). There are also clinically important tuberculous pyloric stenoses, mostly due to ulcers, thickening of the walls (Cordero) and callous (Pfanner). Simmonds, Melchior, etc. described combinations of tuberculous ulcers and carcinoma (G. Frank, lit.).

In miliary tuberculosis, hematogenous tubercles are frequent in the gastric wall, especially in the mucosa. The author saw it chiefly in children with extensive general chronic miliary tuberculosis; verified by Wilms and Simmonds.

Ruge (lit.) reported primary gastric tuberculosis (Alexander), but such cases are always somewhat doubtful. The "tuberculous gastric inflammation, without anatomically demonstrable specificity" as proclaimed by Poncet and Leriche, probably belongs in the known group discussed on p. 712. Literature by Brunner, Gossmann, Zesas, Rother, Biernath.

In typhoid fever, the lymph follicles, the number and extent of which are extremely variable, swell, undergo necrosis and ulceration, but very rarely (Proskauer).

Syphilis of the stomach is quite unusual in adults (lit. in appendix). Gummatous infiltrations with perivascular arrangement and obliterating

vasculitis occur chiefly in the submucosa, but may invade the mucosa, muscularis and serosa. These form elevations sometimes several centimeters in length like plaques or foldings, hard to the touch, eventually followed by pyloric stenosis. Disintegration produces multiple gummatous ulcers often quite shallow (different from simple ulcer) with hard, smooth, bacony bases. Healing by cicatrization occurs perhaps with pyloric stenosis. At times the ulcers and scars are side by side. It is still an open question whether syphilis participates in the development of non-gummatous ulcers, especially the calloused penetrating type (Hausmann). Microscopic investigation should show at least endarteritis and massing of plasma cells (as in Orth's case) to justify a presumptive diagnosis. In congenital syphilis small cell infiltrations are very frequent, but gummatous nodules and plaques are rare (Aristoff, Oberndorfer, lit.). [For clinical and x-ray data, see Eusterman G. B. Am. J. Med. Sci. 153: 21: 1917—*Translator.*]

Herczel reported primary actinomycosis but the case is not clear cut; also Pohl and Hadjipetros, with portal of entry in an ulcer (see lit.). The author saw fistulous perforation into the stomach of a paravertebral actinomycosis.

See Schlagenhaufer in reference to extremely rare lymphogranulomatosis of the gastro-intestinal tract during which infiltrations and ulcers appear. See M. Hoffmann in reference to gastric changes in leucemia and aleucemia. [Hodgkin's disease by Reimann S. P. Cleveland Med. J. 16: 94: 1917—*Translator.*]

### Changes in the Stomach in Poisoning

(Compare chapter on poisoning under mouth cavity (p. 628), and esophagus, (p. 638)

Some of the gastric changes due to poisoning are of purely inflammatory or degenerative type; others depend on corrosion or scab formation, a chemical change producing direct necrosis of parts.

Escharotic poisons may be divided into two groups according to their action:

(1) Poisons which corrode by dehydration and coagulation of albuminous bodies. The architecture of the tissues may still remain; even nuclear staining may be preserved in sublimate or phenol poisoning. But the parts are mostly cloudy, granular and unstainable, although the tissue outlines are still quite discernible; the blood vessels are dilated. Among these poisons are mineral acids, sulphuric, nitric, hydrochloric, which are burning escharotic poisons, also metallic escharotics, as well as phenol and oxalic acid. The first escharotic effect is partly fixative,

partly burning, with a dry, cloudy, more or less deep incrustation of the mucosa.

(2) Among poisons which erode by softening, swelling and liquefaction of tissue are the alkalies, caustic potash and caustic soda. The first caustic effect is clouding, quickly followed by clearing and swelling of the parts which feel soft and soapy (Hofmann, Strassmann). Albumen in liquid combinations is abstracted from the tissues. The alkaline albuminates swell, giving a transparent, gelatinous, soft appearance. The blood pigment is extracted and absorbed by the parietal tissues. The tissues liquefy more when the albuminates dissolve in the presence of abundant water. Caustic alkalies act markedly in the depths and vicinity. Concentrated solutions produce hard crusts.

Microscopic Findings. Sections stain well, blood vessels contracted, connective tissue homogeneous, cell borders obscured, clearing of protoplasm and distortion of nuclei (see experiments of Walbaum).

Inflammatory or degenerative changes alone are seen with diluted poisons, and usually also with arsenic and phosphorus.

When the two latter are absorbed from the stomach, the general intoxication produces injection and ecchymoses of the mucosa, especially with arsenic (arsenic acid), and an added acute fatty degeneration of the glands (with phosphorus); so that the mucosa is thick, cloudy and opaque. But arsenic can cause inflammation and cauterization by its local effects, but mostly superficial, if it remains in one place in the stomach for any length of time. White arsenic granules are octahedral in shape and develop a garlicky odor on burning. They appear microscopically in flakes of bowel contents in arsenical poisoning. In phosphorus poisoning a peculiar garlicky odor and shining fumes rise from the stomach and other tissues.

Concentrated corrosives call forth large scabs (A. Lesser); under them is an active inflammation. The gastric wall, especially the mucosa and submucosa, swell considerably on account of hemorrhagic, serous or even phlegmonous inflammation. This often produces the characteristic picture of large stiff folds, principally in the longitudinal direction, covered on their highest parts by scabs. The effect of these various poisons depends chiefly on the concentration, the amount, and nature of gastric contents at the time of poisoning, and the filling of its vessels; therefore it cannot always be uniform and characteristic. The cauterization scabs even with the same kind of poison vary in color and other characteristics. Black discoloration is due to the blood of the corroded parts.

Corrosive poisons act differently on the blood, and the coagulating corrosives decide the later appearance of the cauterized area by this

activity. Sublimate and phenol coagulate but do not dissolve it, while sulphuric acid, hydrochloric acid, oxalic acid not only coagulate the blood but in a short time change the blood pigment into hematin which causes the scabs to be black brown to black. Corrosive alkalies dissolve the blood which soaks into the scabs and stains them dark tan or black yellow.

Previous therapeutic measures naturally modify the picture seen at autopsy. In grave poisonings with corrosives, death from collapse is usually very quick.

The extent varies, depending on the amount ingested and the distension of the stomach. Sometimes the poison reaches the middle of the greater curvature directly, where it exerts its most marked effect; in other cases the corrosive action is only in the cardia and pylorus while the intermediate parts escape. Sometimes lines or broad tracts correspond to the folds of the contracted stomach and extend from the cardia to the pylorus. But the whole lining of the stomach and even a portion of the small bowel may be uniformly eroded, usually because of much fluid in the stomach; commonly, the most extensive changes are found in the fundus, but the pylorus is involved frequently and not rarely, exclusively.

The latter is indeed very frequent and is explained by the fact that the empty stomach contracts from the irritation, the pylorus is the deepest part, and the lesser curvature is upright.

Strong mineral acids and alkalies cause the deepest ulcers to perforate.

The corrosion continues in the cadaver, and according to Harnac, and Hildebrandt, is indeed much more active on the dead gastric mucosa, so that the changes at autopsy, especially the perforations, as for example, from sulphuric acid causing up to $\frac{2}{3}$ of the stomach to disappear, are post mortem effects. During autopsy therefore, it is wise to look for injection of mesenteric vessels or fibrinous exudate, *i.e.*, plain signs of peritonitis, when the perforation can be considered ante-mortem.

**Fate of Corroded Area.**- If the poisoning does not cause death by its general action, the scabs are cast off by demarkating suppuration. The healing of the ulcers leaves deforming scars and if situated at the cardia or pylorus, must result in stenosis of these openings. In some cases, the stomach shrinks to the size of a fist.

Concentrated sulphuric acid carbonizes the tissues to firm, black, dry, cracked scabs. The mucosa is a remarkably thick, coal-like mass, and in severe cases perforated like a sieve. The acid also carbonizes the blood (p. 673) in the gastric veins which are seen as black stripes. The acid within the vessels penetrates the neighboring organs, especially the omentum, spleen and liver. Perforation of the wall is frequent, but at times is post mortem, (see above). Less concentration may detach the mucosa and form gray white, yellow brown, or light yellow necrotic rags.

Nitric acid produces yellow scabs, if concentrated; otherwise the scabs are brown.

Concentrated hydrochloric acid causes coal black discoloration.

Phenol in stronger concentrations causes a tanned looking scab of white to white red color (the coagulated blood shining through) (characteristic odor of the organs). The erosion is rarely very deep. The same is true of lysol poisoning (50% sol. of cresol; methyl phenol in potassium soap) (lit. by Kathe; Schall). Weak solutions leave no traces in the stomach. So-called phenol (carbol) urine may turn dark gray to black on contact with air.

Sublimate (mercuric chloride) taken directly into the stomach acts according to its concentration and the contents of the stomach. In some cases the solution is absorbed without leaving traces, but in the bowel, especially the colon, there are intense diphtheritic changes. If the stomach is coated with a thick layer of mucus (catarrh, *e.g.*, in drinkers) it combines with the metal to form white mercuric albuminate (insoluble in water); and even after enormous quantities are ingested, the immediate emptying of the stomach may allow recovery to take place. If the mucosa is anemic, the mercury albuminate scabs are white, the living organic albumen combines with the dead metal albuminate compounds and appears like a carbolic acid corrosion, or as if touched with absolute alcohol; usually it is only the upper cell strata which coagulates giving a resemblance to cloudy swelling, but the moisture is absent. In poisoning with sublimate tablets, the epithelium may be stained with the coloring matter of the tablets (*e.g.*, red). If the mucosa was rich in blood the corroded areas are brown. It must be remembered that the metallic salts form first the albuminous combination which is then acted on by the hydrochloric acid (Kobert); this causes inflammatory reactions and changes the blood pigment into hematin. The more intense the corrosion, *i.e.*, the more firm the albuminate scab, the less absorption is possible from the underlying parts. If the scabs are soft the poison and its absorption may proceed unchecked into the depths. More details by Schall; see under intestines and kidneys.

The author autopsied a 30 year old anatomy assistant who had taken with suicidal intent about 8 to 10 gms. of sublimate in 0.85% salt solution on an empty stomach. As soon as vomiting and active, tearing abdominal pains had begun, the man was mistakenly supplied with larger quantities of saline solution and milk later. Death occurred 2 hours after poisoning. The esophageal mucosa, especially the lower portion was thrown off over large areas. The gastric mucosa showed a uniform muco-granular coat, and like the other was dark brown red in appearance. The small vessels of the stomach wall were partly thrombosed, all were markedly filled.

The necrotic detachment of the mucosa in the form of a black brown mushy mass extended to the duodenum, the jejunum and ileum diminishing near Bauhin's valve. The colon showed but slight lesions except for scattered diffuse hemorrhages in the mucosa. Death occurred exceptionally quickly, possibly because of ingestion into an empty stomach, and because of the quantities of saline consumed afterwards. In many cases death does not occur quickly, even after massive doses, because the bichloride does not dissolve completely or because a protective layer is produced. A 24 year old man took 15 tablets each 1 gm., in water and died in 48 hours; a nurse took 10 tablets each 1 gm., and an unknown quantity of morphine, and died on the 4th day. The lethal dose according to Kobert, is 0.18 gms.

The general effect of sublimate poisoning is quite as inconstant and uncharacteristic when absorbed by the genital organs, skin or abdominal cavity, etc. Not rarely there are hemorrhages and erosions of the mucosa. In one case the author saw yellow white dots due to calcium granules in the epithelium.

Silver nitrate causes white, violet, or under the influence of light, black scabs.

Preparations of copper such as copper sulphate, verdigris, etc. stain the gastric and intestinal mucosa green (vomitus is green) but it turns deep blue on treating with ammonia. In chronic poisoning by verdigris (copper line on teeth) as from the use of copper kitchen utensils, severe dysenteric changes are found in the gastro-intestinal tract.

Oxalic acid and its potassium salt produce white superficial necroses or, after longer application, green, yellow or black from hematin formation. The white cloudy deposits (also on the intestinal mucosa) consist of precipitated calcium oxalate (amorphous or crystalline) and are quite characteristic (see under kidneys).

Cyanide of potassium acts like potassium hydroxide on the stomach, but with the blood pigment (also post mortem) it forms a striking red to blue red combination (cyanmethemoglobin, Kobert). The change is very characteristic (according to Hofmann); the mucosa becomes soapy, slippery, blue red or brown red, covered with blood stained mucus, swollen, and transparent on the upper parts of the rugae. The changes are only hyperemia and ecchymosis; the rest is post mortem. If the loose combination of potassium cyanide is broken up by the acids of the gastric juice, the corrosive character disappears and hydrocyanic acid produces an internal asphyxia of organs in the presence of excess of oxygen. The light red cadaveric spots are cyanmethemoglobin. The specific odor of the acid can be detected in the organs.

Vegetable poisons are without important or characteristic effects. The stomach frequently participates in the general congestion of the asphyxia, produced by the action of these poisons on the nervous system.

**Round Gastric Ulcer—Chronic—Simple—Perforating Digestive Ulcer**

Compare digestive ulcers in the duodenum, esophagus, jejunum, colon and after gastro-enterostomy, where they are usually single, and obscure as far as their primary cause is concerned. Peptic jejunal ulcers show a marked tendency to extend deeply and cause acute symptoms by perforation, and the chronic symptom of intense pains (lit. in appendix). Peptic ventricular ulcer also occurs spontaneously in all domesticated animals, but

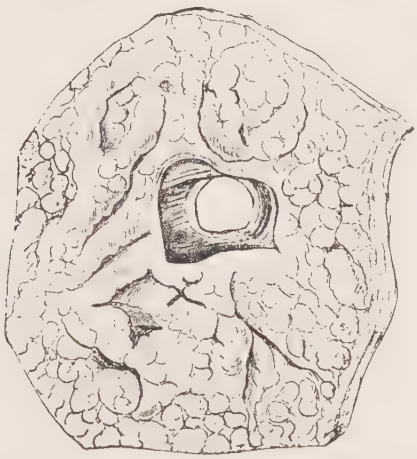


FIG. 293.—Round gastric ulcer, deep, perforated with large opening. The layers of the stomach wall are as though carved out. Mucosa of stomach shows chronic granular gastritis ('etat mamelonne'). Man of 60 with verrucose endocarditis; nat. size.

rarely becomes chronic (Joest, Spez. pathol. Anat. d. Haustiere, Vol. I, 2nd half, 1919).

**Pathogenesis.**—The ulceration is caused by digestion by the gastric juice, and Stuber (see lit. p. 685) has shown that tryptic gastric ulcers can also be produced (for trypsin, see under pancreas).

The process is analogous to the development of hemorrhagic erosions; in the latter the mucosa is saturated with blood, undergoes necrosis and is thus vulnerable to the gastric juice; in simple ulcers various local nutritional disturbances occur in the gastric wall; the mucosa, deprived of its nourishment, has its vitality lowered and is dissolved by the gastric juice. This causes a defect devoid of reaction, which heals completely, or progresses into the depths to perforation, or, prevented by various factors from healing, becomes a typical chronic ulcer.

The causes of ulcer are not alike.

Nutritional disturbances in the stomach wall are probably due most frequently to vascular changes, *i.e.*, thrombosis, arteriosclerosis (lit. Buday, Hamburger), and according to the author's experience it explains the ulcers which appear in men of advanced age, as verified by Ophuls, Kelling, Reeves (lit.) and especially by Hart, Krompecher (lit.). Krompecher also thinks of constriction of the small vessels of the mucosa caused by the pull of a filled and over-stretched stomach. In rabbits by intravascular injection of formol, Payr succeeded in producing endarteritis and endophlebitis followed by the formation of ulcers and spontaneous perforation; F. Rosenbach produced the same with several injections of adrenalin. Congestive hemorrhages cause erosions, and hemorrhagic and simple necrotic infarcts occur in the embolism of endocarditis, atheroma of the intima and venous embolism (p. 664); these may become ulcers. Blood changes are also suspected as in chlorosis, giving insufficient nutrition to the wall. According to Stoerk, decreased resistance of the mucosa and increase of follicles may be a result of the lymphatic constitution; other causes are arterial spasm (see ulcer in plumbism, Schiff; v. Ortner), chronic gastritis (Nauwerck) and lesions of the mucosa from hot food or mechanical insults, but these lesions usually heal quickly (Gross, Bottcher). The same holds good of hemorrhages with subsequent ulcers after blunt trauma to the abdominal wall (Stern, Thiem, Dietrich). Roessle thinks of local ischemia of the mucosa induced by the sympathetics and secondary digestion. The spasm or neurotic theory (v. Bergman) states that spasm, especially of the muscularis mucosae (Lichtenbelt), causes ischemia which is the precursor of ulcer formation, and anemic or hemorrhagic infarction of the mucosa. Chronic spasms cause chronic ulceration since they prevent healing and cause fresh ischemia. But v. Bergmann also recognizes the importance of vasomotor spasm and spasm of the muscularis propria for the chronicity this is the mechanical factor (see below), along with nutritional injuries (curative success of milk diet!). For increase of ulcers during the war, see Schwarz. v. Bergmann also accepts Rossle's opinion, which states that ulcers are secondary diseases, *i.e.*, with sources in the peritoneum, the appendix, gall bladder, hernia operations, etc., which irritate nerve tracts and transmit pathological vagotonic reflexes to the wall of the stomach (and the duodenum) with subsequent circulatory and nutritional disturbances, erosions, and finally ulcers (see Gruber lit., criticism of this theory). Hart also emphasizes the importance of reflex peripheral and central nerve stimuli. Nicolaysen advises microscopical investigation of the vagus. v. Bergmann's theory of musculo-spastic conditions due to increased vagotonus (supported by Gundelfinger) is attacked by others including Haller (experiments) and Schwarz, who believe that ulcers in vagotonic individuals

merely cause exceptionally severe irritative symptoms. Stierlin considers the problem far from explained because of the contradictory experiments concerning the gastric innervation. Neumann emphasizes a mycotic origin (Bottcher); in animals, Rosenow succeeded in producing typical chronic ulcers by the intravenous injection (embolism) of streptococci from human ulcers; see p. 688 in reference to thrush infection of chronic ulcers. Ulcers are said to select anemic chlorotic young women, but our pathological anatomical statistics do not verify this statement; indeed in 139 cases at Basle, the author found men and women equally affected, and in reference to age, 35 cases occurred between 21 and 50 years, while 88 cases over 51 years; Oberndorfer in Munich gives similar statistics. For later statistics from Basle, see Schonberg, (lit. appendix). Spiegel thinks that gastro-intestinal diseases are frequently present in families of ulcer patients, especially carcinoma of the stomach, and he sees this as a proof of constitutional organic factors in the etiology of ulcer. According to Bartel, ulcer is frequent in the lymphatic constitution (p. 678).

Hyperacidity of the gastric juice is frequently seen in ulcer but not always; indeed, according to v. Bergmann, not even in one-half of the cases. Many lay great stress on this finding and consider it both of importance in the development of the ulcer, *e.g.*, when in chlorosis the blood alkalinity is reduced coincident with an accidental lesion of the gastric mucosa, and in delayed healing, the real characteristic of chronic ulcers. For this reason the excess of gastric juice was thought removed by doing a gastro-jejunostomy and according to A. Kocher this is a good procedure for all ulcers (disputed by Stromeyer) whether of the pylorus, fundus or lesser curvature. Weintraub affirms that insufficient mucous coating is a reason for the chronicity of the ulcer, and by experience it is known that substances which actively increase mucus secretion (argentum nitricum) favor healing. But the author often observed a very thick mucous covering in resected calloused ulcers. Aschoff, Stromeyer and others consider chronicity of the ulcer due especially to its location in the gastric furrow because there the contents are retained longer and the mucosa is subjected to constant mechanical disturbance (tension, friction, pushing) during contractions; this is a chronic, chemical-mechanical irritation of the ulcer once formed. Consequently three conditions are said to be necessary for the formation of a chronic ulcer: defect, localization in the gastric furrow, and the action of functional anatomic factors (Bauer, lit.). According to v. Bergmann, chronicity is essentially due to spasms, which in turn are constantly induced by the ulcer in a vicious circle (Spiegel, Reinhard). Matthes, also Payr (p. 678), succeeded in producing ulcers somewhat similar to those in humans, but in most experiments the established

defects healed quickly without ulcer formation; for ulcers due to injury of the celiac axis, see lit. in appendix.

The macroscopic appearance of a simple ulcer is very characteristic, especially if small and deep, (fig. 293). Approximately round or oval in shape with flat sharp margins without any reaction whatsoever, the ulcer penetrates funnel-shaped, becoming narrower, obliquely in steps or terrace-like arrangement. It is smaller in the muscularis than in the mucosa

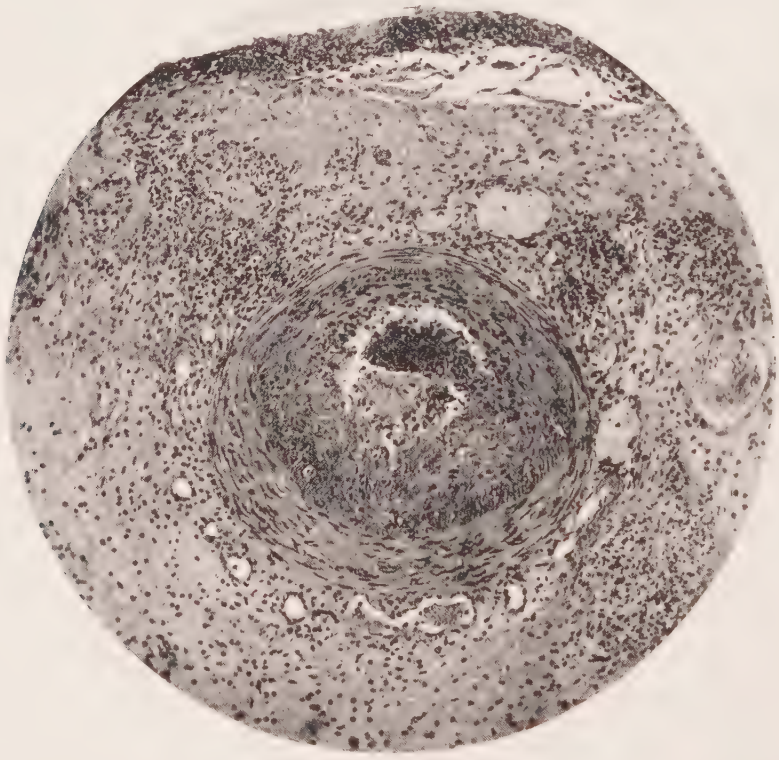


FIG. 294.—Thrombosis of vessel in the wall of a gastric ulcer. Some believe such vascular changes are the fundamental causes of the ulcer; others believe these are secondary. It is difficult, if not impossible, to decide in most cases. Quite probably this is secondary since vessels not far away showed no such lesions. × 130. L. H.

and smallest in the serosa. All this is less sharply defined in larger and shallower ulcers (fig. 298).

According to Stromeyer and Aschoff, the characteristic form, with the apex of the funnel directed toward the cardia and the step arrangement in the part of the circumference toward the pylorus, is produced essentially by the action of tension and friction and not by the direction of vessels.

The base of the ulcer is first dirty brown, but it soon becomes quite clean and the layers of the wall appear as though carved out. In old

ulcers, the scar tissue sometimes smooths the ridges and almost obliterates the layers. But in other cases, especially in hypertrophic gastritis, old ulcers are quite deep, 0.5 cm. and more. This is made possible by a calloused thickening of the stomach, chiefly of the muscularis, and often also by an overhanging proliferating adjacent mucosa bulging over the edges

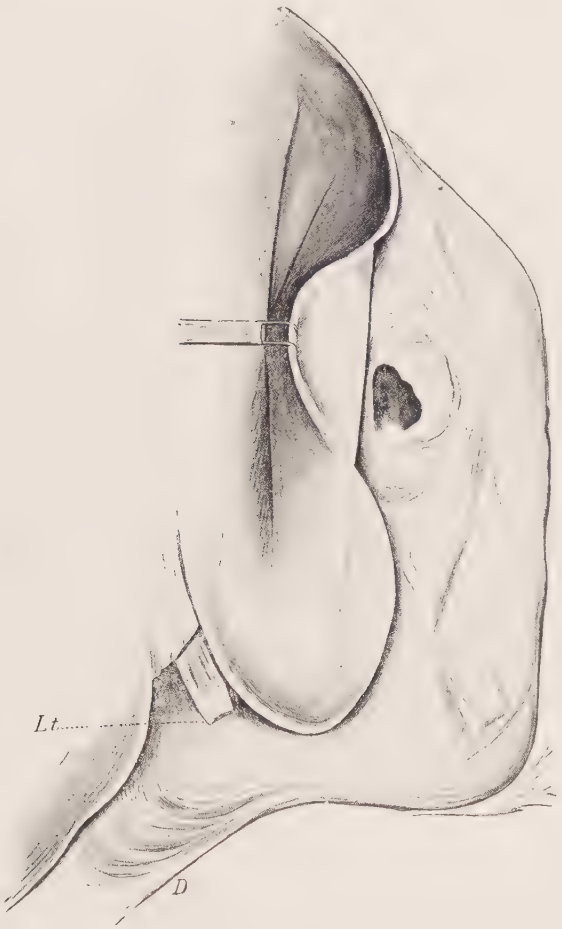



FIG. 295.—Perforated chronic gastric ulcer revealed after lifting up the left liver lobe which was attached to the vicinity of perforation by fibrin and pus in the neighborhood of the small curvature. Lt, lig. teres; D, duodenum, drawn in situ; 19 year old servant girl had gastric pains, and acid eructions. Perforation with sudden great pain in l. side; death 36 hours later of general fibro-purulent peritonitis (bac. coli); $\frac{2}{3}$ nat. size; comp. with Fig. 297, belonging to this.

(especially in cardia ulcers). This causes the apparent depth of the calloused ulcer (figs. 293–297).

The microscopic findings in a fresh ulcer are very negative. Besides slight small cell infiltration of the marginal areas, only the lesion is seen. Indeed at the beginning even the infiltration is absent, and the ulcer is

hardly distinguishable from an artefact; the changes become more decided as time goes on. Younger and older connective tissue extends inward more or less deeply; a very vascular granulation tissue, obliterating endarteritis (and phlebitis), and neuritis are found in the close vicinity. The margins of the lesion may be covered with fibrin, injected with blood and show marked small cell infiltration and necrosis in spots (signs of progressive ulceration). For more details, see Askanazy. For healing by cicatri-

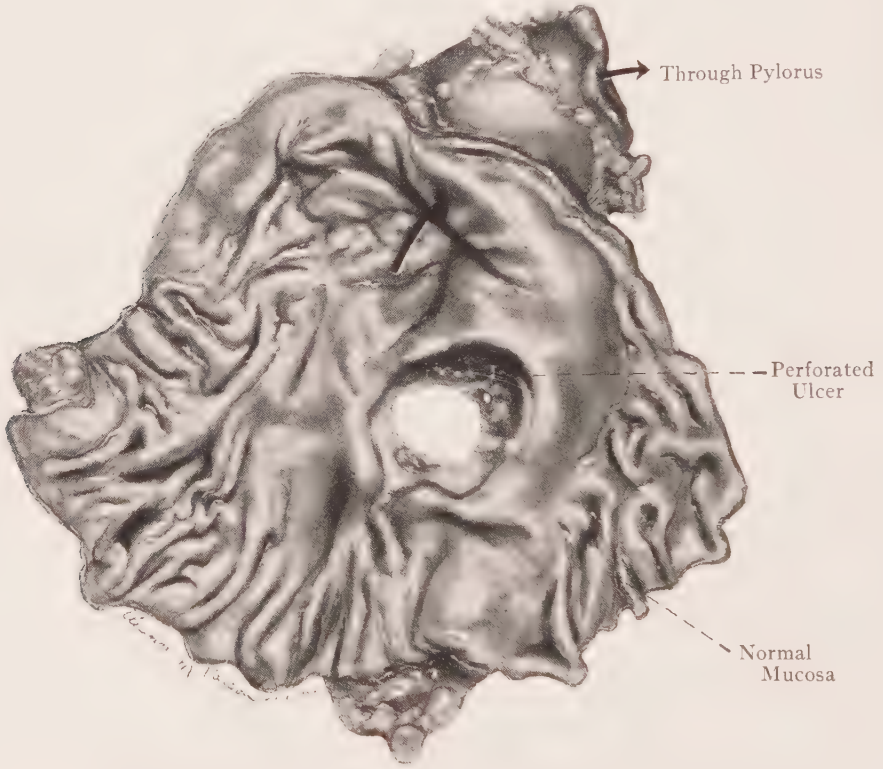



FIG. 296.—Chronic benign gastric ulcer, perforated, on the lesser curvature near the pylorus from a patient 36 years old. Operative specimen. According to the history, this ulcer had been present for 10 years. Its rims were hard and calloused and it proceeded funnel-shaped through the wall to the perforation as shown. The perforation was well walled off by adhesions to the under surface of the liver so that general peritonitis was avoided. This is termed chronic perforating ulcer as distinguished from the acute variety with sudden violent onset and sudden devastating pain and shock. The latter are much more prone to produce general peritonitis because of the absence of protective adhesions. L. H. #19882.

zation, see p. 687. The size of the ulcers varies between 0.3–1.5 cm. to the size of a small plate, but larger ulcers are rare, usually shallow, and rounded, and not rarely straddle the lesser curvature. Large ulcers may be confluent adjacent ulcers. Symmetrical ulcers occur from embolic occlusion of both forward and backward limbs of the coronary artery; they are saddle shaped or like the figure "8."

Places of predilection are the posterior wall, near, or on the lesser curvature; next in the region of the pylorus. According to Jatrou, the region of the so-called gastric pathway is poorer in vascularization and anastomoses than the rest of the stomach, and besides, according to Hofmann and Nather, the vessels are more delicate and more readily compressed where the muscularis is most markedly developed. The cardiac area and the fundus, the anterior wall, and the greater curvature are chosen less frequently. Adjacent ulcers of the duodenum and of the pylorus may blend by undermining the pyloric ring, thus producing a gastro-duodenal fistula. Usually but one ulcer is present, but not rarely there are several, often one after the other in a row (fig. 292, p. 662). Fre-

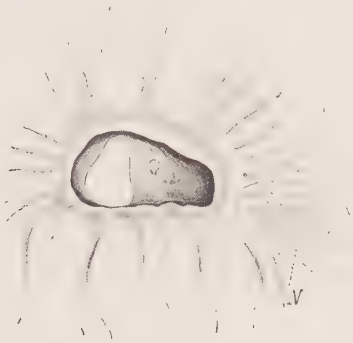



Fig. 297.

Fig. 298.

Fig. 297.—Deep perforating gastric ulcer. Inner view of ulcer illustr. in fig. 295. In the indurated ulcer base two small humps are seen corresponding to larger vessels of the muscularis. N, sacr; ⅔ nat. size.

Fig. 298.—Flat round gastric ulcer with ruptured aneurysmal artery (A) (coron. ventr. sup. left) in base; death by exsanguination, man 74 years old. Ulcer in posterior wall of cardia; also an ulcer scar in the hypertrophic pyloric end; ⅔ nat. size.

quently, old scars are found besides fresh ulcers (fig. 297). See Bauer for localization of ulcers.

Perforation. Acute ulcers, often not larger than a nickel, may progress through the wall to perforation perhaps in a few days (primary perforation, or acute perforating ulcer).

Strong contractions or pulling of the stomach from over filling may complete the perforation of the last thin serous layer.

This allows escape of the gas-containing stomach contents, unless previous adhesions to adjacent organs prevent it.

Sudden sharp pain in the epigastrium, pressure pains, board-like rigidity of the abdominal walls (defense musculaire), vomiting (not always), are the first clinical symptoms.

Death usually results, sometimes before general peritonitis sets in. The opening is about the size of a lentil, and in typical cases is circular or oval and sharp edged, as though made with a punch, (Rokitansky).

Viewed from the mucous surface, the loss of substance appears much larger and the ulcer margins narrow toward the outside in the form of a flat funnel. Location of predilection, as in fig. 295, is on the anterior wall near the lesser curvature toward the cardia, covered by the left lobe of the liver; perforations of the posterior wall are much rarer. Multiple perforations

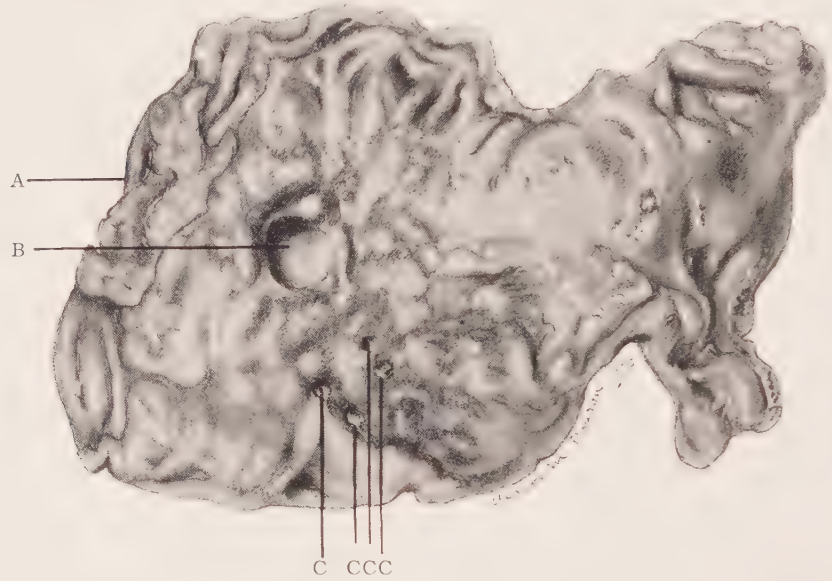



FIG. 299.—Gastric ulcer on the posterior wall near the pylorus. (A) Pyloric end; (B) chronic ulcer; (C) multiple early ulcers. In interpreting specimens like this, it is impossible to begin without careful study of the patient's history. The relationship of subjective troubles to the specimen can many times be worked out to an astonishing degree. On the other hand, it is only fair to restate the old adage that human testimony is fallible and too much reliance cannot be placed upon history. The reason for the pain and ofttimes absence of pain in the presence of gastric ulcer is worthy of a chapter by itself. Suffice it to say that pain may or may not be present in the presence of ulcer. There is no doubt from the appearance and the histological study that the ulcer marked (B) is old. It is cup-shaped, its margins are hard, somewhat overhanging, calloused, tough, comparatively avascular. The small ulcerations at (C) are more or less rounded, punched out, and extended, at the time the specimen was removed, only through the mucosa. In all probability had this specimen not been removed, some of them would have healed; whether any would have become chronic, calloused ulcers, is impossible to say. The study of specimens of this type should do much to clear up many of the vexed points in relationship to this common and very important disease. In discussing its pathogenesis, too much stress cannot be laid upon the fact that the clinical diagnosis, even with the help of the x-ray and other means, is not infallible and so deductions based on clinical observations must be regarded with due caution. L. H. #19131.

sometimes occur (details by Brunner, F. and G. Gross). Spontaneous healing of a perforation is very rare, (Wagner, lit.).

In other, far more frequent, cases the ulcer spreads slowly peripherally and downward—chronic ulcer; in approaching the serosa it stimulates strands or bands, or broad, flat adhesions to adjacent parts (adhesive peritonitis), pulling them firmly up against the stomach. This ulcer often causes severe cardialgias.

Responsibility for the pain has been laid to neuritic changes and to pressure on nerves in the ulcer from scar tissue (see Nissen and especially Askanazy, who described neuromas).

Ulcer scars may be present alongside the ulcer (fig. 297 N). When perforation occurs, the stomach contents may spread between adhesions or into an adjacent organ, or directly into the peritoneal cavity with subsequent general peritonitis (fig. 295).

The larger the quantity of gastric contents that escape, the greater the danger. Sometimes escape is prevented by the left lobe of the liver which is plastered over like a lid, (fig. 295). Perigastric, encapsulated, gas-containing abscesses develop between the spleen and diaphragm and eventually are called subphrenic abscesses, etc. (p. 233). But these are more frequent from duodenal ulcers and appendicitis. The capsule is formed by organized fibrinous exudate.

The pancreas is frequently in the bottom of a chronic ulcer, but it is very resistant and rarely undergoes marked peptic destruction. The edges of the base of the ulcer are plastered shut to the pancreas which is the granular, nodular, yellow base with its lobules separated by cicatricial strands (fig. 300) which must not be mistaken for carcinoma! Other ulcers burrow into the liver as deep cavities the size of a fist. More rarely they tunnel into the parenchyma of the spleen. The author saw a case in Breslau in which the base of a crateriform hollow in the spleen had eroded a branch of the splenic artery leading to sudden fatal hemorrhage.

Among the rarer perforations may be mentioned: through the diaphragm into the chest cavity (pleural cavity, lungs, pericardial sac), very rarely into the gall bladder (Rindfleisch), oftener through the abdominal wall (as seen by the author in a 59 year old woman), even through the umbilicus (external gastric fistula). Somewhat more frequently they rupture into the bowel as internal gastric fistulae or bimucous fistulae, chiefly into the duodenum or colon; in the latter case the feces contain much poorly digested food. This is called "lientery" (smooth, *i.e.*, undigested feces).

Ulcers of the anterior gastric wall, even if chronic, are more subject to perforation (general peritonitis) than those in other regions, possibly because access to mechanical injury and greater motility prevent adhesions in these parts. The perforation is very typical, as illust. in fig. 295.

Perforated gastric ulcers are very rare in small children (Bechthold, lit.). [Perforation in utero, Lee, W. E. and Wells, J. R., Ann. Surg.: 36: 1923.—*Translator.*]

Hemorrhages from gastric ulcers are greatly feared, whether as repeated hematemesis causing inanition, or massive, causing quick death.

The smaller hemorrhages from chronic ulcers are very frequent; larger hemorrhages come chiefly from eroded larger arteries in the base of an ulcer and in the stomach wall, or frequently in adjacent organs. Sometimes the ulcer is quite small. The author saw a case in which a very minute opening was found in a branch of the left superior coronary artery in the base of a rounded shallow lesion of the gastric wall, barely the size of a lentil; it caused the death within 4 days of a 19 year old girl. It may also happen that the bleeding ulcer or the vessel within the small ulcer cannot be found at first; attempts can be made to find it by squeezing the base of the ulcer or by injecting water into the aorta above while it is held shut below the coeliac artery. Sometimes a sort of preparation

FIG. 300.—Deep chronic gastric ulcer exposing pancreas, and broad erosion of aneurysmal splenic artery which disappears to the left in a folded scar.

for rupture occurs thus: first the adventitia is infiltrated by round cells, causing nutritional disturbance to the media and intima sufficiently severe to allow rupture by necrobiosis or by the peptic action of the gastric juice. Sometimes the ruptured vessel is aneurysmal (see figs. 298 and 300). The arteries are chiefly coronaries (fig. 298), the splenic (see fig. 300) and the gastro-duodenal. The vessel is perforated above or laterally, or is completely separated. See p. 688 in reference to erosion by the thrush fungus.

Rupture of a branch of the coronaries causes a crossed hemorrhage from both sides because of the anastomoses. Venous hemorrhage from the stomach wall, or from arteries and veins simultaneously, or from a large neighboring vein, *e.g.*, the splenic, is rare.

**Healing by Cicatrization.**—Healing occurs in the majority of cases; a flat ulcer is covered with connective tissue and epithelium and becomes quite smooth, leaving only a flat rounded spot. But more frequently there is a permanent white, flat, rounded, or stellate scar in the mucosa which, in retracting, pulls in the adjacent mucosa in prominent radiating folds. If the muscularis suffered deep destruction the scars are much more apparent and contracted, but all scars are much smaller than the original ulceration. Sometimes ulcers and scars are found side by side (figs. 297 and 300).

The deeper the ulcer the more the cicatricial contraction. If a granular gastritis is also present, the scars appear especially deep. If the gastric wall is perforated and the base of the ulcer is in an adjacent organ, the mucosa may be pulled over the margins and inverted (fig. 300).

The extent and location of scars determine changes in shape of the stomach. Hour glass stomach, a contraction oblique to the long axis, can be developed during the existence of a calloused ulcer by spasm (spastic hour glass stomach) or by an anatomically spastic lesion, *i.e.*, spasms added to an anatomical narrowing, or by perigastric adhesions, corrosions, malignant neoplasms, etc. (Veyrassat, lit.). Stenoses at the fundus, cardia or pylorus are frequent; the latter causes dilatation and often remarkable muscular hypertrophy up to 1 cm. in thickness. Sometimes the stomach is shortened by a helix-shaped rolling in of the lesser curvature so that the cardia and the pylorus approach each other. In the presence of several constrictions, saccular or diverticulum-like ectasias may develop (Kleine, Schlesinger, Borsceky).

In the scars and borders of ulcers, microscopic gland remains are sometimes visible and also extensive proliferations of more or less atypical heterotopic glands (Hauser; p. 666). It may be accompanied by round cell infiltrations, occasionally with many eosinophiles.

Carcinoma may develop in scars (Hauser) or in still existing chronic ulcers, (p. 709). According to Hayem and Konjetzny, the atypical proliferations within the edges of pyloric ulcers may change into carcinoma, as repeatedly seen by the author. Statistics in reference to ulcer carcinomas vary from 2 to 80% (lit. by Anschutz and Konjetzny; Gruber, Konjetzny, Pauchet and Delort). On the other hand, a peptic ulcer may develop in a slow growing carcinoma, and as the author pointed out in the 2nd edition, it is difficult to determine which is the primary change; a most careful macroscopic and histologic investigation may decide (Ad. Schmidt, Hauser, Verse, Stromeyer, Gruber, Konjetzny). A simple calloused ulcer and an ulcerated carcinoma usually cannot be distinguished absolutely (lit. by Faulhaber and v. Redwitz; v. Haberer).

Askanazy calls attention to the almost constant presence of thrush in chronic gastric ulcers; it is thought that this infection makes healing impossible, or at least difficult. Nissen denies this statement; the question requires further investigation (v. Meyenburg); Pick, and later in more detail Askanazy (lit.), described arterial erosion due to the thrush infection.

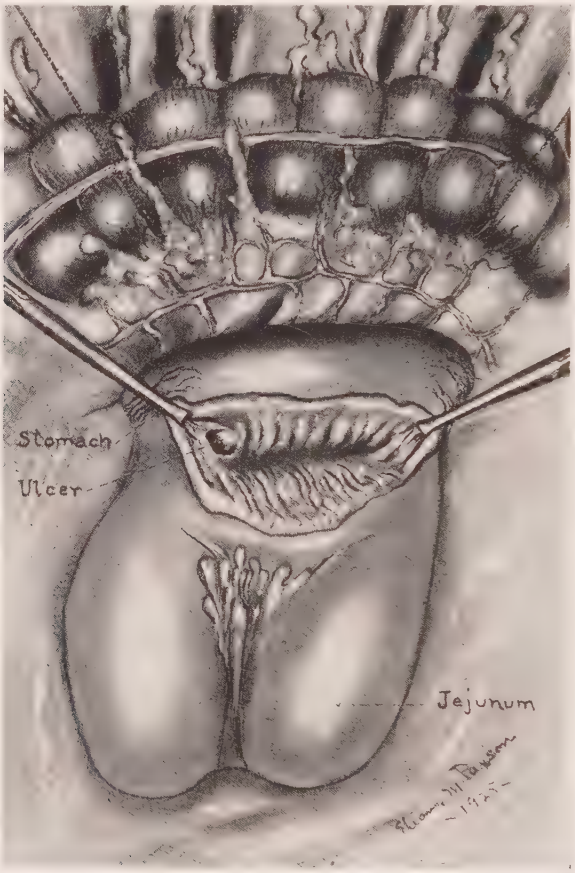



FIG. 301.—Marginal ulcer at the site of an old gastro-jejunostomy. This complication of the latter operation is dreaded. They produce recurrence of the old symptoms. They have a tendency to hemorrhage and considerably more tendency to perforation. Their pathogenesis in certain cases has been traced to faulty operative technique such as allowing pieces of linen thread, etc. to remain in the opening. In other cases they arise, in all probability, as a result of the original causes which produce the ulcer for which the operation was performed. L. H.

Diseases of the stomach due to mould fungi (aspergillus fumigatus, etc.) are rare. Marchand and Beneke each observed one case with dirty brown to black pulpous gangrenous ulcers quite different in appearance from typical round ulcers. See also cases of Ljubimowa, Benelli, Chiari, lit., Teutschlander, Menzinger, Lohlein, v. Meyenburg, lit.; the latter

saw ulcers due to hyphomycetes which showed a tendency to quick encrustation; there were "metastatic" liver abscesses. [For lit. of peptic ulcer, see Karsner, H. T., J. A., M. A. 85: 1376: 1925.—*Translator.*]

**Translator's Remarks.**—The literature of few subjects is so beset with divergent opinions as that of peptic ulcers. Not only do surgeons and internists approach the subject from different points of view, but surgeons and internists differ radi-

FIG. 302.—This remarkable specimen came from a man 25 years old. He had been shot in the abdomen eight months previously and had recovered without operative help. He soon complained of severe stomach disturbances and finally discovered a mass in his epigastrium for which he came for relief. At operation this mass was found to be hard, dense, quite freely movable and attached to the posterior wall of the stomach. This was resected together with a portion of the posterior wall of the stomach. It showed the ulcer as in the illustration. The mass was composed histologically of ordinary fibrous tissue. Embedded in the mass was the bullet. The cause of the excessive formation of connective tissue in the form of a tumor-like cantaloupe-sized mass is unknown. Patient made uninterrupted recovery. L. H.

cally among themselves. The points of view of pathologists depend to some extent on the relative amounts of surgical and autopsy material which they examine, *e.g.*, the relation of ulcer to carcinoma which is discussed above. Certainly, surgeons have contributed much to our knowledge of the disease and have also stimulated much of the experimental work. From the translator's experience, mostly surgical, but also autopsy, the most significant statement in the text above is that the cause of

ulcer is varied. As far as the development of carcinoma in ulcer is concerned, he believes it is impossible at present to determine this accurately, chiefly because of the unreliable nature of human testimony (history), the great difficulty of accurate clinical diagnosis (in spite of modern aids, much of the literature is worthless because the patients who were studied were not shown to have ulcers by operation or autopsy) and the impossibility of predicting what would have happened if the surgeon had not removed the ulcer, *i.e.*, if it would have become a carcinoma.

### Tumors of the Stomach (Lit. by Konjetzny)

**Benign tumors** are only exceptionally of importance. One form is encountered quite frequently, namely:

The so-called mucous polyps, not actually frequent, but occurring (*a*) in chronic hypertrophic gastric catarrh, usually grouped most thickly in the pyloric region and not separable from polypoid gastritis (p. 667); and (*b*) independently from unknown causes (developmental disturbances?). If very numerous they are called "ventricular polyposis" (polypoid gastritis, adenomatous polyposis).

FIG. 303.—A, diagram of adenoma, and B, of a cylindrical cell carcinoma; a, b, c, mucosa, muscularis, serosa. The benign tumor A, grows upward (t), does not transgress the border of the muscularis mucosae and submucosa; carcinoma (B) also grows upward (t) but in addition invades the depths to the serosa.

In (*a*) they appear in the form of tumors consisting essentially of mucous tissue, beet-like or broad based, pedunculated, usually small, the size of lentils and peas, but occasionally larger. Connective tissue and muscularis mucosae form the core covered by convoluted, hypertrophic, often cystic glands. On section they are usually moist, glassy, gray red. They can be called simple (or inflammatory) mucous polyps, and are found chiefly in older individuals.

In (*b*) adenomatous polyps are composed essentially of proliferated mucosa glands covered with a single layer of cylindrical epithelium with many goblet cells. Perfect uniformity of the epithelium does not exist; indeed these benign epithelial tumors show a certain degree of polymorphism.

The gland formations sometimes consist essentially of elongated tubules, sometimes very irregular in construction, much convoluted and lobar on section; the glands are often cystic.

They are usually small, solitary, but sometimes multiple (adenomatous polyposis), in the latter case combined with a much more marked intestinal adenomatous polyposis, usually in young people; more rarely they are

large, flat or pedunculated. On section they are gray white, cloudy, marrowy, finely porous or small cystic. The core thickly infiltrated with round cells may show marked papillary branching. These are simple, cystic and papillary adenomas (fig. 303-a).

In contradistinction to carcinomas, adenomas show no tendency to disintegration, but exceptionally they are ulcerated by peptic digestion. But carcinomas may develop in them, whereupon the proliferating cells produce quite atypical new forms. This is rare in the stomach as compared to the intestines. An adenoma may grow in the presence of a carcinoma (v. Saar), but rarely as compared to the frequency of adenomatous polyposis and carcinoma in the intestines.

The interstitial tissue of these polyps often contains many hyalin bodies, non-nucleated, staining shiny red with eosin, of various sizes, sometimes of mulberry shape. Lewy thinks they are coagulation products of tissue fluid and has described them in chronic gastritis; Schirren, who thinks they are derived from erythrocytes, found them in atrophy; v. Hansemann, etc., in polyps; Thorel, Lubarsch, Bleichroder (lit.) believe they are derived from the granules of acidophilic cells (Fabian, also Saltykow, Path. G XII, 1908 and discussion).

Rarely, there develop soft, villous, vascular, elevations of the mucosa covered with simple cylindrical epithelium, eventually as large as a fist and tending to hemorrhages—papillary fibroepitheliomas—villous tumors —papillomas.

Larger papillomatous tumors prefer the pyloric region and have been known to cause invagination of the stomach (Chiari).

This tumor examined superficially may be mistaken for villous carcinoma, but it does not penetrate the deeper layers like carcinoma (fig. 303-b) but grows from the mucosa into the stomach cavity, while its lower boundary, the muscularis mucosae, is not crossed, apart from small irregularities due to pulling and pushing of the growing parts. If it crosses, it is a malignant tumor which of course may also grow upward, but, to make its malignancy clear, it penetrates downward without regard to tissue boundaries (fig. 303-b). A malignant tumor always shows a tendency to disintegration.

Nodular fibromas, white, fibrous, hard, eventually calcareous or juicy, are very rare. Bircher described a pedunculated external gastric fibroma as large as a man's head; others project internally like polyps (lit. by Konjetzny). Lipomas from submucous or subserous fatty tissue, are usually small and of no importance. Neurofibromas (neurinomas), multiple, external on the stomach and intestine, are rare, (Askanazy); neurofibromatosis (see under nerves) may be present at the same time. Myomas and fibromyomas occur close to the cardia, in the middle portion

or pyloric region, rarely at the pylorus (Lotsch), and are often multiple, mostly small; but the author saw a pendulous fibromyoma approximately as large as a hen's egg in a woman 66 years old, a finger's breadth from the cardia, and a smaller one alongside. Lotsch saw a pyloric myoma the size of a goose egg, with invagination of the duodenum. A similar case is described by Nenke. In addition to these internal intramural and submucous, sometimes polypoid and pedunculated fibromyomas (in rare cases bleeding, Miodowski, B. Fischer), there are similar tumors externally, sometimes pedunculated, occasionally multiple, rarely very large, to the size of a man's head (Steiner, Hake, lit.). Both are equally rare, favoring women and advanced age. In a 56 year old woman the author saw an exceedingly firm tumor, as large as a child's head, weight 2325 gms., attached externally to the lesser curvature by a broad base; it had turned the stomach on its long axis and pushing downward lay over the pelvic opening and simulated an ovarian tumor. There had been discomfort for ten years before the severe symptoms of incarceration due to the axis torsion. Lit. by Mouriquand and Gardere, Hauswirth, Albu, Konjetzny; v. Hansemann described a "pure" myoma which metastasized to the liver and pancreas; biologically, this is a so-called malignant myoma (p. 693).

Lymphangiomas in lacunar form make the mucosa uneven; cavernous angiomas are blue red and lobulated; both are rare. Occasionally an aberrant pancreas, even the size of an almond, is encountered (see under pancreas). Josselyn de Jong described formations like tumors in the pyloric region consisting of hyperplasias of Brunner's glands.

**Malignant Tumors.**—Carcinomas and sarcomas occur. The latter are very rare, the former exceedingly frequent.

Primary sarcomas are very rare (Schlesinger, Pstrokonski and lit. in appendix). They start in the submucosa (most frequent) and muscularis, more rarely from the subserosa and mucosa. They are nodular, broad-based or pedunculated tumors outside the stomach, exogastric, or in the wall, intramural, or on the inner surface, gastric or endogastric. Stenosis is rare (*e.g.*, in one of Schlesinger's cases). Sarcomas which occupy chiefly the inner layers sometimes are nodular soft infiltrations and if, as is most frequent, they are round cell types, it may be very difficult not only macroscopically, but also microscopically, to differentiate them from round cell carcinomas. But they do not select the pylorus so frequently; they are oftener a clinically demonstrable tumor, show less tendency to ulcerate, are less malignant, and usually of longer course; sometimes they reach the size of a man's head and a weight up to 12 pounds which never happens with carcinomas. In a soldier 32 years old the author saw the inner surface of the stomach covered by immense, nodular, fairly firm, tumor masses covered with smooth mucosa which almost filled the lumen, the

only exception being a small area in the fundus; a continuation of the tumor, as large as a fist, invaded the liver, another the diaphragm toward the right lung; lymph node metastases were absent histologically,—polymorphocellular round cell sarcoma.

Intramural round cell sarcomas may grow very rapidly and soften in the center to form occasional abscesses, rupture into the stomach cavity, suppurate and even lead to fatal hemorrhages. The author described (C. f. Schw. 1906–17) such a tumor as large as a child's head in a 51 year old woman (A. Staehelin, lit.). In other cases spindle cell sarcomas, hard fibrosarcomas, rare myxosarcomas, mixed cell sarcomas and angiosarcomas occurred.

The author saw an exogastric, pendulous, firm, spindle cell sarcoma the size of a chestnut as an accidental finding in a 79 year old man, and

FIG. 304.—Pendulous sarcoma, (spindle cell sarcoma), externally on the stomach. Accidental finding in man 79 years old; 7/8 nat. size.

he investigated a pedunculated exogastric myxosarcoma of similar size in a 52 year old woman; the latter tumor had undergone cystic softening from hemorrhage and necrosis and was adherent to the omentum. It was removed from the stomach. Most cases occur between the 5th and 6th decades; men and women are about equally affected (Hesse). Sometimes young individuals, even children, develop lymphosarcomas which are hardly less frequent than round cell sarcomas; the greater portion of the inner gastric surface may show small nodules; frequently the organ is dilated, but it may be narrow (nodular stomach) (Saltykow, Hesse). Sarcomas may also develop from fibromyomas. In the outer gastric layers of a 70 year old woman, the author found a nodular submucous fibromyoma with central calcification, barely as large as a chestnut, and a sarcoma springing from blood vessels (perivascular spindle cell sarcoma) with an hepatic metastasis of the same structure, larger than a child's head. In other cases sarcomatous transformation of myomatous parts is seen (myoma sarcomatodes; more details under uterus; so-called

malignant myoma). The author observed such a tumor as large as a child's head in a 55 year old man with enormous metastases to the liver (H. P. Hosch, lit.; see under liver). Cases reported as endotheliomas of the lymph vessels must be viewed with scepticism; the author never saw such a tumor (consult Krompecher-Makai, lit.; Ribbert). Silvan described an intravascular hemangio-endothelioma which appeared like a linitis plastica. Metastases appear in $\frac{1}{3}$ of the cases, most frequently in regional lymph nodes and the liver, but occasionally in other organs, including the skin (lit. by Hesse).

Secondary sarcomas are less rare, usually multiple, of the types melanotic, round cell, more rarely spindle cell. They are usually situated in the submucosa, or mucosa, their shape is coin or beet-like, the surfaces are slightly hollowed, like a saucer.

It must be remembered that leukemic infiltrations may simulate a true neoplasm, especially if disintegrated.

**Carcinoma** of the stomach is a malignant neoplasm springing from gland epithelium, more rarely from the mucous surface epithelium, from adenomatous polyps, atypical gland proliferations, or gland remains in ulcer scars.

In 1078 carcinomas in Basle and 836 in Gottingen, they occupied first place in frequency of all autopsy carcinomas, with 28.66% and 37.22%. Other statistics, as for example, those of Reiche, reach 50%.

**Development and Local Extension of the Tumor.**—The gland cells and the glandular membrana propria proliferate; they retain their gland characteristics more or less, or lose them promptly; utilizing the lymphatics (Cuneo), they penetrate in hollow tubules or solid plugs, into the muscularis mucosae and submucosa. The nests anastomosing with each other at first spread actively, and then enter the muscularis and serosa, but also the mucosa, above and peripherally, destroying the glands (Borrmann). But Hauser has shown that during peripheral extension, carcinomatous changes occur in the glands of adjacent parts (Petersen and Colmers, Verse, Tsunoda). It is certain that multicentric development is frequent, sometimes indeed from almost all the glands in the entire stomach wall (v. Rindfleisch), while in other cases th development is unicentric (Borrmann). Multiple primary gastric carcinomas are very rare; most likely they arise from polyps as the author has verified (Schneider, lit.). Progressive invasion of very atypical epithelial forms from the level of the mucosa into the deeper layers of the wall, eventually as far as the serosa, is one of the characteristics which distinguish carcinoma from the heterotopic gland proliferations in chronic gastritis (p. 666) and especially from benign glandular neoplasms or adenomas (fig. 303-a and b).

Among developmental causes it is assumed that the basis may be laid in some cases by chronic gastritis, especially the polypoid forms (Konjetzny, lit.), and the heterotopic gland proliferations of chronic gastritis mentioned on p. 666 are other important starting points. Carcinoma can doubtless develop in an ulcer, ulcer scars (p. 687) and from transformation of adenomatous polyps. But on the whole, it develops

Fig. 305.—Adenocarcinoma of stomach, can be called microcystic cylindrical cell carcinoma a, mucosa; b, submucosa; at c this is penetrated by the pseudo-glands of the carcinoma; d, cystic adenocarcinomatous proliferation in submucosa and muscularis, their borders are blotted out; (med. magn.). II. Section of pseudo-gland of adenocarcinoma. Several layers of irregular cellular coverings arranged around a lumen; mitotic figures. (High power.)

from unknown causes. Males are more predisposed; in 309 gastric carcinomas in Basle (28.66% of all carcinomas), 168 were in men and 141 in women. In 312 cases of gastric carcinoma in Gottingen (37.22% of all carcinomas), 226 or 72% were in men. The ages 50 to 70 are criticial (I. Diss. Krasting). Cases occurring before the 30th year are rare; but in a woman only 21 years old the author saw an infiltrating carcinoma on the greater curvature which had developed in the scar of an ulcer

(p. 709) and an 18 year old girl (I. Diss. Bernoulli) died of hemorrhage from a carcinomatous ulcer. There are cases reported in younger individuals (*e.g.*, Karl, 9 year old boy); they run a rapid course, cause many metastases and high fever (Schlesinger; Libienthal). The duration of the disease is about 2 years and it is often accompanied by extraordinary loss of weight.

Histologically and macroscopically, four main forms of primary carcinoma of the stomach may be recognized to which the rare primary squamous cell carcinoma may be added.

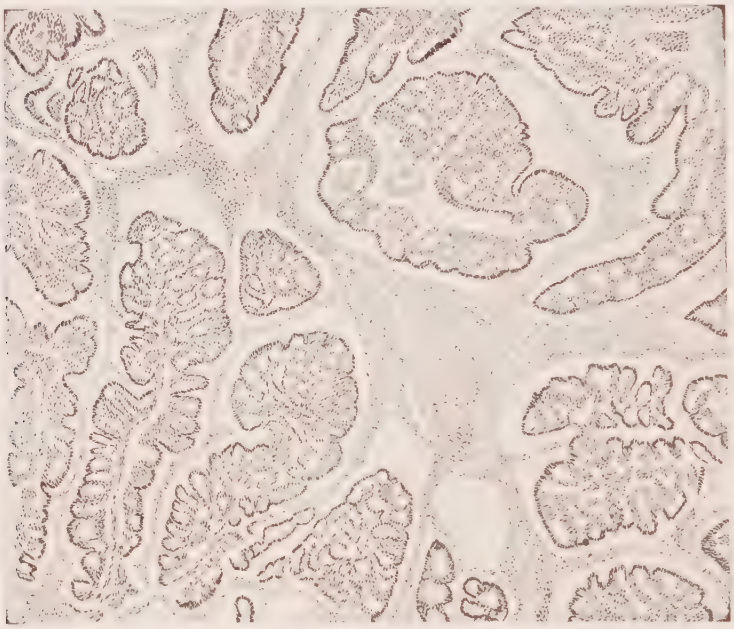


FIG. 306.—Adenocarcinoma with larger, complicated, perforated, gyriform gland-imitations; some lumena contain secretion. Interstitial tissue shows small cell infiltration. In between fragments of muscularis from sigmoid. Man 56. (Low power.)

The following classification has been useful to the author in his practice for many years but it must be understood that the designation of the separate forms is meant "a potiori;" transitions from one to another occur quite frequently.

**Cylindrical Cell Carcinoma.**—(1) The glandular form—adenocarcinoma; (2) solid cylindrical cell carcinoma; (3) papillary cylindrical cell carcinoma.

(1) **Microscopical Characteristics of Adenocarcinoma.**—Starting from the cylindrical epithelium of the glands, this tumor produces atypical, misshapen imitations of glands surrounded by an alveolar scaffolding, and proliferates both upwards (like adenomas) as hollow tubules or solid

plugs from the tubules like buds, and downward into the depths of the wall which is the characteristic of carcinoma. The tubules are longer, broader and deeper than normal gland tubules. The cellular lining may consist of several layers, see fig. 305 II, but often is composed of only a single layer (fig. 311-b); the cells are usually of different sizes and not regularly arranged side by side; their nuclei lie at different levels and stain more intensively than those of normal glands. But in some places the gland imitations may be so natural that they suggest a benign cylindrical cell adenoma (see fig. 305 under rectum). The cells of these neoplastic gland tubules may produce serous fluid by which hollow spaces

FIG. 307.—Solid cylindrical cell carcinoma of ileum. Firm tumor, size of a thumb-joint causing stenosis in girl 19. The peripheries of the nests show cylindrical cells, otherwise polygonal. Indication of gland-like formation of hollow spaces; m, muscularis. (Medium magn.)

or small cysts are formed (microcystic cylindrical cell carcinoma) (Hauser). Adenocarcinomas in which the gland imitations are larger, scalloped, more complicated and gyriform, etc., are seen much oftener in the colon than in the stomach (fig. 306).

(2) In the solid cylindrical cell carcinoma (Hauser), solid nests appear, in which the cells touching the surrounding connective tissue are arranged cylindrically and in palisades while the interiors of the nests consist of rounded or polygonal cells (fig. 307). This form might be classed with the basal cell carcinomas of the cylindrical epithelial mucosae (Krompecher); they are rare but there are combinations of (1) and (2). The fungoid cylindrical cell carcinoma is macroscopically a soft, solid, or polypoid papillary tumor with a tendency to grow upward. The region

of the pylorus is the site of election. The surface shows very finely dotted, porous characteristics due to gland imitations, as though it had been pricked by a pin; sometimes larger gland lumenae are seen (microscopically cylindrical cell carcinoma). Sometimes the tumor tissue is homogeneous, dense, and macroscopically not distinguishable from a solid medullary carcinoma. If the tumor disintegrates, which may occur rather late, dainty bowl shaped ulcers are produced, shallow, or crateriform or deep with thick fungoid everted overhanging edges. These ulcers may perforate. Perhaps metastases are not as frequent as in other forms. The

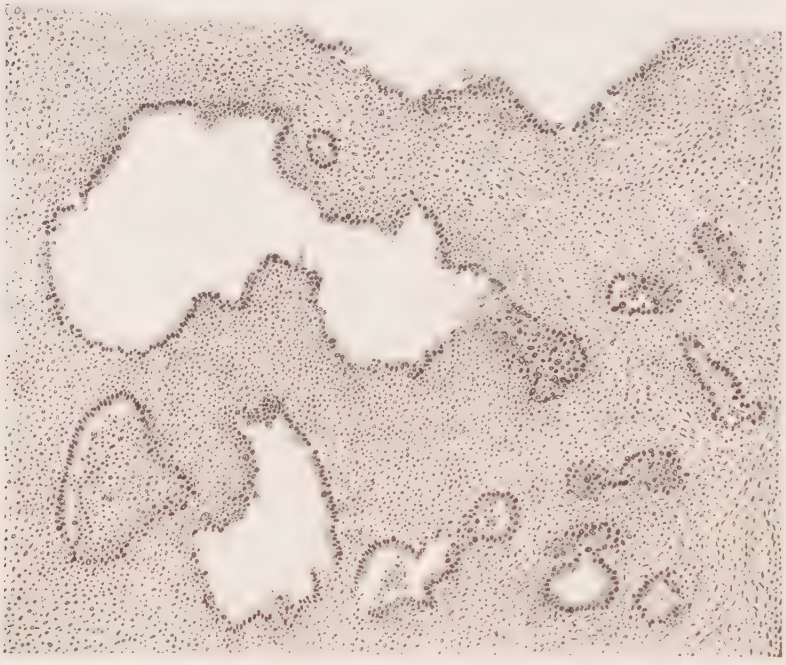


FIG. 308.—Granulomatous carcinoma of stomach (lesser curvature) of woman of 68. Granulation tissue destroyed the pseudo-glands of an adenocarcinoma.

regional lymph nodes are infiltrated relatively late and often only to slight degrees. This again is evidence for the assertion that a carcinoma is the less malignant the higher developed the epithelial character of its cells.

(3) The rare villous carcinoma (carc. papillosum; see fig. under bladder) is a papillary cylindrical cell tumor starting from the surface epithelium and can be recognized as carcinoma only on cross section. As far as it grows upward in the form of branching villi covered with cylindrical epithelium it resembles a papillary fibroepithelioma, but the epithelium assumes atypical forms, grows down into the tissues and spreads by continuity to its surroundings, *e.g.*, into the liver (Matsuoka).

Soft, medullary, cylindrical cell carcinomas are accompanied by extensive granulation in the interstitial tissue with numerous leucocytes, small and large lymphocytes, eosinophiles and plasma cells; the author repeatedly saw destruction of the primitive gland imitations, erosion of the carcinoma bodies and infiltration of the cell nests (fig. 308). This carcinoma granulomatosum was also seen by the author in the mammary gland, larynx, etc. It might be mistaken for a carcino-sarcoma. Ribbert described similar findings in lymph nodes, (Konjetzny).

**Solid Globo-cellular Carcinoma** (*Medullary Carcinoma*).—The designation "medullary" means brain-like, soft, dense, homogeneous.

**Microscopical Appearance.**—The cellular constituents preponderate in comparison with the stroma. The cells are fairly small and irregular, but still approximately rounded, although sometimes polygonal from mutual pressure; they are not dissimilar to lining cells, but probably are not derived from them, but from cylindrical epithelium, the newly formed cells remaining at a lower developmental stage, *i.e.*, a sort of indifferent form. Occasionally the polymorphy is marked and the name polymorphocellular solid carcinoma may be applied; individual cells may be quite large. The cells grow rapidly in solid masses and plugs, upward and downward, and follow the lymphatics into the depths as far as the serosa, (fig. 310). The principal growth is very often in the submucosa (fig. 310-d), and thick layers may spread over wide areas under an intact mucosa. The stroma then consists only of a delicate scaffolding which may be entirely overlooked in thicker sections. Its meshwork is close (small alveolar round cell carcinoma; fig. 309), and the cells lie in strands one after the other; or very large corresponding to the size and luxuriance of the epithelial filling (large alveolar round cell carcinoma; fig. 310).

The infiltration may become so diffuse that the alveolar structure remains visible only at the margins. The author saw such carcinomas with marked polymorphy; the large cells with large nuclei and polynuclear giant cells in large numbers resembled those of sarcomas which however, have larger and brighter nuclei. Such forms might be called polymorphous and large cell, round cell carcinomas.

Macroscopically two basic forms of medullary carcinomas are differentiated:

(*a*) A soft, irregular bulging, but sometimes rounded globular or ovoid-shaped tumor appears most frequently at the cardia and sometimes spreads over the greatest part of the gastric mucosa. It grows quickly, enters the submucosa, and unfolds its development in the lymph channels and thus progresses to the peritoneum (fig. 310) where it is elevated into large and small bosses. It rarely causes diffuse infiltration of the peritoneum.

This carcinoma soon undergoes ulcerative disintegration and is in part digested by the gastric juice. It also undergoes suppuration since the hydrochloric acid production is often diminished or absent, and decomposition follows. Marked fat metamorphosis is also frequent. The carcinomatous mass has a very thick wall, often smooth and still covered with mucosa. Hemorrhages are frequent, but gross erosion of the gastric or splenic arteries with fatal hemorrhage is rare. On account of its marked vascularity (arteries, capillaries and especially veins), the medullary carcinoma was formerly spoken of as "fungus hematodes" or "telangiectatic carcinoma." Invasion of neighboring organs is rapid such as to the liver, pancreas, and it perforates the colon, duodenum and ileum, usually after adhesions have formed. Metastases are rarely absent

Fig. 309.

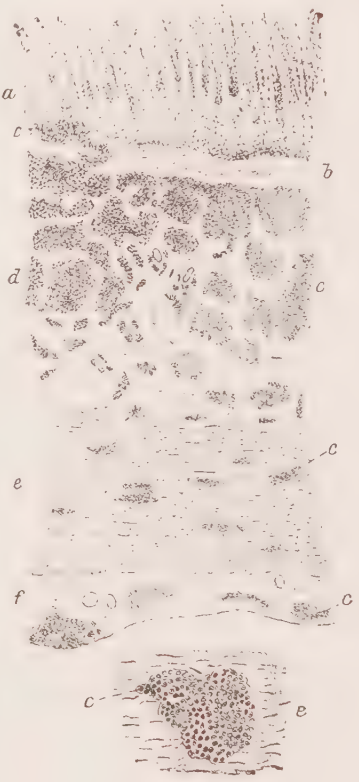



Fig. 310.

Fig. 309.—Small alveolar round cell carcinoma; medullary carcinoma of stomach. Some of the cells have fallen out. The loose cellular union is an artefact due to imbedding in paraffin. (High power.)

Fig. 310.—Solid large alveolar globo-cellular carcinoma; medullary carcinoma of stomach penetrating the whole wall. a, mucosa; b, muscularis mucosae. Masses of carcinoma c, especially in the submucosa in large heaps d; in one place cells penetrate the muscularis mucosae and invade the mucosa; e, circular and longitudinal muscle containing some nests; f, serosa, also with nests; (low power). The small picture shows a solid (round cell) carcinoma group in the muscularis (high power).

in adjacent lymph nodes and they are frequent in the liver, lung, intestinal serosa, etc.

(*b*) Medullary carcinoma may occasionally show pure infiltrative growth, especially in the mucosa and submucosa, but sometimes it invades all layers and the stomach wall reaches a thickness of several centimeters. The infiltrated mucosa has stiff, thick, smooth bosses and folds. Ulceration is at times confined to a relatively small area.

Corresponding to its cellular and imperfect epithelial structure, medullary carcinoma is very malignant.

**Scirrhous Carcinoma. Carcinoma Fibrosum.**—This is a deviation of the cylindrical cell and the solid globo-cellular and may combine with the colloid.

The designation "scirrhous" suffices for the macroscopic description, but not for its microscopy. First, the carcinoma parenchyma must be

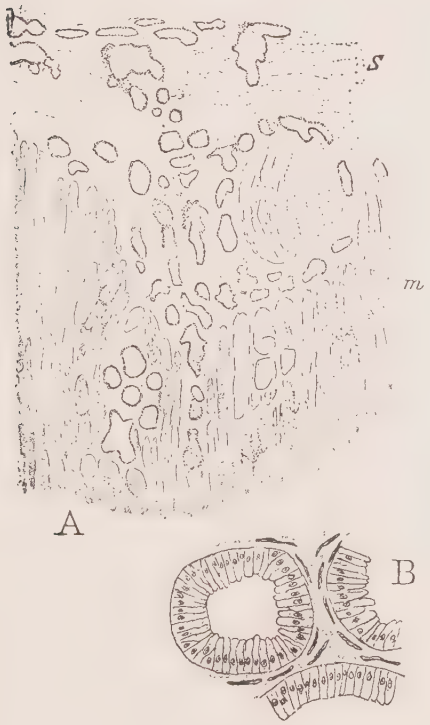



Fig. 311.

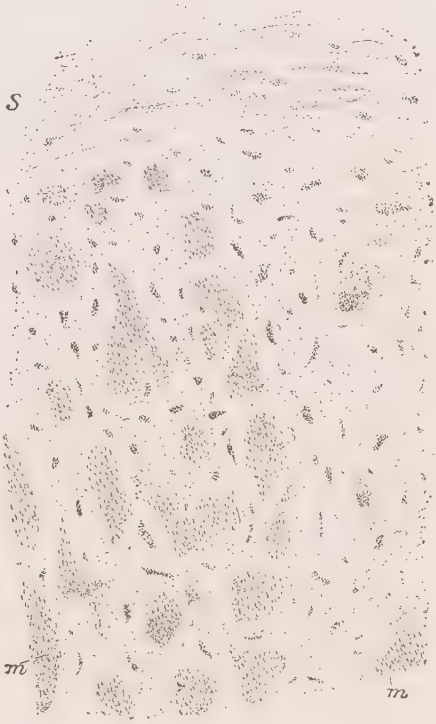



Fig. 312.

Fig. 311.—A, from a stenosing scirrhous carcinoma of pylorus; S, submucosa and m, muscularis invaded by scirrhous adenocarcinoma (fibrous). The gland imitations of carcinoma are sparse and surrounded by much connective tissue. B, good gland imitations from an adenocarcinoma; lining of one layer of not quite regular cylindrical cells; cells partly displaced; nuclei not always at same level. Detail of A.

Fig. 312.—From a stenosing scirrhous carcinoma of the pylorus; s, submucosa; m, muscularis (circular layer). The solid nests surrounded by much cellular connective tissue are mostly small, round celled (solid scirrhous globo-cellular carcinoma) and usually form an apex; on the right, above, are larger nests; the hypertrophic muscularis is also invaded and forced apart. (Low power.)

arranged in a special way and second, the stroma must be quite dense to merit the designation "scirrhous." Thus, *e.g.*, macroscopic scirrhus of the pylorus; microscopic scirrhous adenocarcinoma or scirrhous globo-cellular solid carcinoma, etc.; *i.e.*, "scirrhous" by itself means nothing of the character of the decisive epithelial part.

**Microscopy.**—The cells recede behind the connective tissue stroma with its tendency to shrinkage. The cells sometimes are arranged in tubules like adenocarcinomas (fig. 311), only there are less of them, and they are surrounded by much connective tissue. But more frequently there are solid nests of polymorphous round epithelial cells penetrating the wall. These nests may be larger or smaller, and accordingly differentiation is made between large and small alveolar solid scirrhus. In the latter, the infiltration is but slight, and difficult to distinguish from the common round cell infiltration of chronic gastritis unless the polymorphous and often vacuolated cells are carefully studied. This is the more difficult, because nests or cells are almost destroyed by fatty degeneration, vacuolization, nuclear disintegration and shrinking (local healing), and nothing remains but contracting tangled, fibrous stroma. Pathologists are long acquainted with these "healing processes," (compare atrophic cancer, Virchow, Konjetzny; see p. 668). Still more difficult is the histological diagnosis of certain small cell scirrhous carcinomas called by Krompecher and Makai according to their microscopical impression, "carcinoma disseminatum;" the carcinoma cells do not form true firm groups, strands and nests, but loosely scattered cell masses; often actual single cells lie in clefts and cracks of the connective tissue. This form was mentioned in discussing "plastic linitis" (p. 668). Not rarely the carcinomatous character is recognizable only in the peripheral parts (the youngest) of the tumor. It is thus clear that there are scirrhous varieties of cylindrical cell and medullary round cell carcinomas, etc.; scirrhosis develops whereever the connective tissue shows extensive proliferation around tumor nests. The carcinoma cells or their chemical products are said to stimulate this tissue overgrowth, and like all scar tissue, it shrinks; with the many new elastic fibers (as in the case in fig. 316) (Meinel) this shrinkage and contraction causes atrophy of the carcinoma cells but unfortunately, as a rule, the growth of the tumor as a whole is not halted.

Scirrhous carcinoma grows slowly, is most frequent at the pylorus where it may remain localized for a long time without forming adhesions to adjacent tissues. It leads to hard infiltration of the walls, especially the submucosa which may reach a white tendinous thickness of 1 cm.; the glassy translucent muscularis, especially the inner circular layer, hypertrophies to a marked degree; white strands pass through to the serosa (fig. 317). The hypertrophy may account for one-half of the thickening. The serosa is wrinkled, folded and covered with nodules; adhesions to surrounding parts may be inflammatory or neoplastic; the motility is curtailed. The epigastric lymph nodes are hard and infiltrated. But in some cases, there are no adhesions or infiltrations, and the carcinoma is confined to the pyloric region which it obstructs with the usual subsequent

dilatation of the rest of the stomach. Sometimes the carcinoma spreads through the whole stomach wall and the organ may be smaller than a fist, rubbery, hard and flat (like a canteen, fig. 316). The mucosa may be remarkably smooth, but thick, rigid and firmly attached to its base, or more or less deeply ulcerated, as hard as cicatrized tissue. The ulcerations have hard discolored bases and flat rims. Scirrhous carcinoma also infiltrates the entire peritoneum; especially the omentum and mesentery

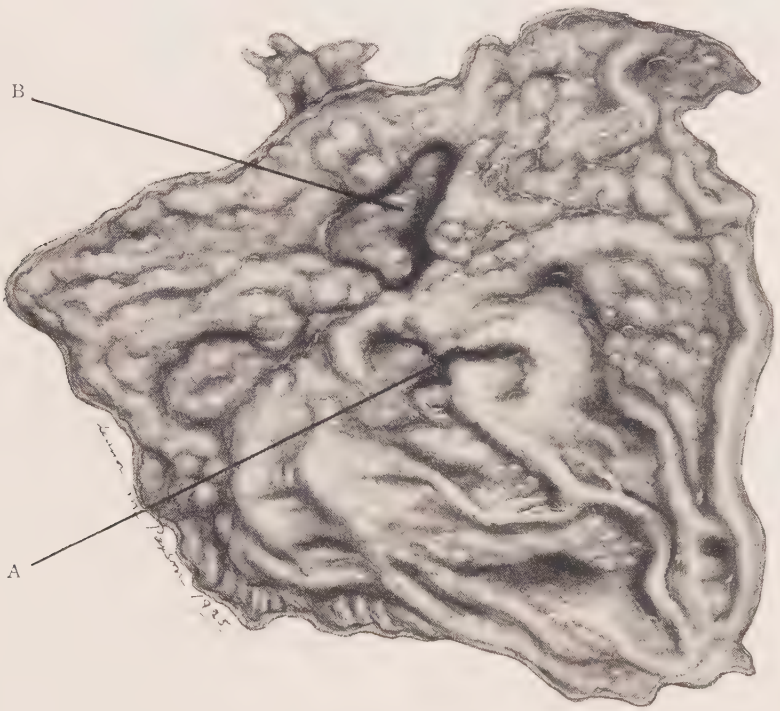



FIG. 313.—Carcinoma of the stomach. Observed on opening the stomach. (A) Pyloric opening. (B) Ulcerating carcinoma. These, but more especially those of rounded contour, have led to the supposition of the development of carcinoma in an ulcer. As stated in the text, the exact number of ulcers which become carcinomatous is problematic and cannot be determined. Many of the harder, scirrhous types of carcinoma show a hard marginated wall with a dirty gray ulcerating base. L. H. #19102.

of the small intestine are much shrunken and shortened (see under peritoneum).

When closely confined to the pylorus, the tumor at times is difficult to recognize; we may hesitate between scirrhous carcinoma, chronic gastritis with hypertrophy of the pylorus and chronic ulcer. Careful examination of the serosa (nodules) and lymph nodes is very important, because some well defined, soft, tumor masses may be found, while the stomach wall has only traces of the infiltration.

Some are of the opinion that lymph vessel endotheliomas or even so-called benign pyloric hypertrophy (Meinel) may be masked by the picture of diffuse scirrhosis with intact mucosa (Cignozzi, lit.); but scepticism is in order.

**Colloid Carcinoma.**—A variation of the cylindrical and the globo-cellular.

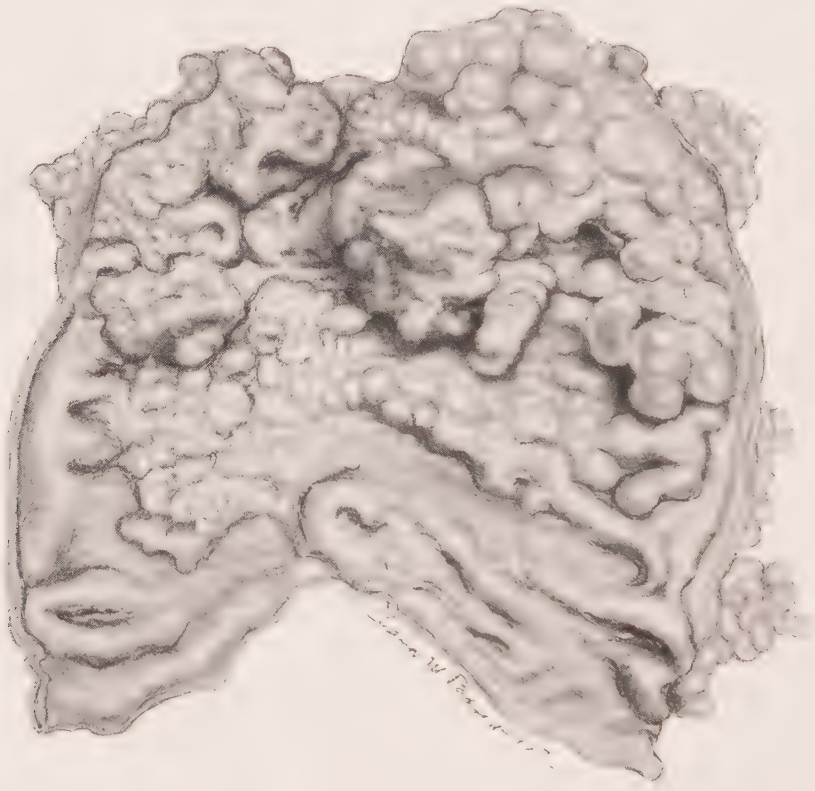


Fig. 314.—Polypoid carcinoma of the stomach. Operative specimen from a man 42 years old who complained of stomach trouble for 6 months. In the center to the left is an area of ulceration, the only one present. Extension has occurred through the stomach wall and to one adjacent lymph node but at operation no metastases were found in the liver or other organs including lymph nodes in the vicinity. Microscopically this was a papilliferous type of adenocarcinoma with a tendency to the production of considerable mucus. L. H. #1029.

**Microscopical Conditions.**—This form is a variation of the round cell or cylindrical cell tumors, due partly to the presence of mucous secretion from cylindrical cells in goblet cells and gland-like lumina, and partly (more frequently) to mucoid and gelatinous swelling of the protoplasm and the nuclei of the cells. The mucus fills the cells, the cells disintegrate (fig. 315-b) and the debris becomes confluent. It may occur to all the cells of an alveolus which then contains only mucus, or to only occasional cells. The gelatinous substance is almost concentrically layered. When

the septa undergo the same change, the confluent alveoli may become very large (macroscopic). The mucin itself may swell; it stains characteristically with thionin or polychrome methylene blue. There also occur rare scirrhous colloid carcinomas.

The metastases may show the primary character of cylindrical cell carcinoma or more frequently round cell medullary carcinoma; like the

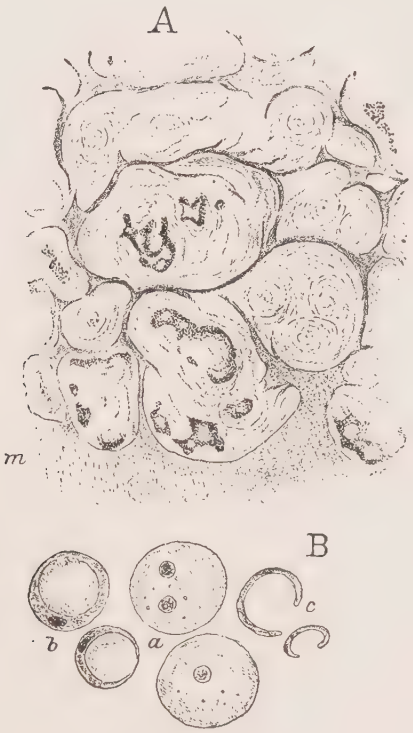



FIG. 315.—A, Colloid carcinoma of stomach; large alveoli filled with colloid substance arranged partly concentrically; dark areas within composed of round epithelial cells (medullary carcinoma); m, muscularis. (Low power.) B, Phases of colloid formation in epithelial round cells; at b, droplets within the cell (seal ring forms); at a, cells quite colloid, but containing nuclei; c, remains of cells resembling open rings, from which the colloid has separated. (High power.)

latter, the colloid carcinoma grows rapidly and shows a tendency to diffuse infiltrating extension.

Thus colloid carcinoma infiltrates diffusely, especially around the pylorus but perhaps also through the whole stomach. The stomach wall reaches a thickness of 3 cm. or more; the bosses on the serosa are transparent. Usually the alveolar structure can be recognized macroscopically, the yellow or brown gelatinous contents shine through the delicate dividing walls and on section slowly well out. The stomach, completely infiltrated, is small, often markedly so, although never as small as in scirrhous

carcinoma. Ulcerative destruction of the lining always has colloid bosses, nodular, and smooth, as though scraped. Perforation is rare. The lymph nodes and more distant metastases occasionally consist of mucus without trace of cells, but, as in other carcinomas, secondary growths may be completely absent. Extensive infiltration of the peritoneum is common, and the scirrhous forms are often combined with the colloid, naturally, since cylindrical cell carcinoma and medullary carcinoma may change into colloid carcinoma as well as into the scirrhous tumors. Massive, vascular, transparent, firm tumor growths are especially frequent in the omentum which thickens to a large bulk, and because of scirrhous changes, shortens and rolls up. The whole peritoneum may have immense gelatinous nodules or diffuse infiltrates everywhere. Ascites is prompt and frequent.

**Rare Forms.**—Primary squamous cell carcinoma is rare in the stomach and occurs usually at the esophageal border. The author described a large carcinomatous tumor of the posterior gastric wall of a 42 year old man as a cornifying squamous cell carcinoma with infiltrations progressing to the liver and gradually disappearing at the esophageal border (Herxheimer).

Kulbs described ciliated epithelium in a gastric carcinoma and its metastases.

Rare carcinomas with sarcomatous character of the stroma (lit. by Lindemann, Konjetzny) are called carcino-sarcoma or carcinoma sarcomatodes. The author has seen a few. They are not to be mistaken for granulomatous carcinoma!, see fig. 308.

**Macroscopic Appearance and Course of Carcinoma of the Stomach in General.**— Carcinomas grow with varying rapidity; the harder forms more slowly, generally speaking, the more cellular and softer forms more rapidly. The carcinoma at first infiltrates the mucosa and muscularis; the latter, as a rule, hypertrophies, but finally atrophies from increased invasion. From the muscularis the tumor reaches the serosa. According to the form, nodular and diffuse, annular and insular, non-ulcerated and ulcerated tumors may be distinguished. Saddle-shaped, rarely perfect annular carcinomas, usually beginning in the lesser curvature, may cause deep constrictions or hour-glass form of the stomach. Diffuse carcinomas cause thickening of the walls; if of the whole stomach plus scirrhous shrinking, the volume of the stomach is reduced. The so-called canteen stomach is the outstanding type (fig. 316).

The collection at Basle contains a carcinomatous stomach of the hour-glass type, the size of two chestnuts, the walls 1 cm. thick.

Diffuse carcinoma in the pyloric region (fig. 317) (the most frequent site of carcinoma of the stomach) may cause stenosis and dilatation and hypertrophy of the stomach with its sequelae. Carcinomas are frequent also

in the posterior wall and the lesser curvature. In the cardia (fig. 318) they may extend to the esophagus or along the lesser curvature. Stenosis of the cardia reduces the size of the stomach and causes dilatation and hypertrophy of the esophagus. Carcinomas of the greater curvature are relatively rare. The tumor on the inside of the stomach is subject to disintegration, fatty degeneration, necrosis and the action of gastric juice; ulceration is often purulent. The ulcers are cup-shaped with bulging rims because the tumor continues to extend peripherally while the ulceration destroys the central parts (fig. 382). They may perforate into adjacent

FIG. 316.—Scirrhous round cell carcinoma of the whole stomach wall with marked increase of elastic fibres; bottle-stomach, capacity 270 cc. from woman of 74. Inner surface of stomach partly smooth, partly shallow ulcerated; dense carcinomatous infiltration of omentum (N); infiltration and stenosis of esophagus (O); D, duodenum. Diffuse carcinomatosis of peritoneum; marked ascites; gastric symptoms (vomiting) for only a few weeks; ⅔ nat. size.

cavities or organs (peritoneum, intestine, especially the transverse colon, liver, pancreas, spleen, etc.) and even through the abdominal wall.

Perforation due to peptic digestion is distinguished by a small sharp edged puncture in the serosa.

Vascular carcinomas bleed readily and freely, and lead to hematemesis, but erosion of larger vessels is relatively rare.

A tendency to diffuse infiltration is characteristic of some carcinomas, especially the solid globo-cellular tumors and the scirrhous and colloid variations; others (adeno-carcinomas) show a tendency to form circum-

scribed nodules and to ulcerative disintegration. Diffuse infiltrations and nodules both produce stenoses.

In tumors of the pyloric region the stomach commonly is ptosed.

Usually the pylorus acts as a sharp boundary line toward the duodenum, but the author saw cases in which the carcinoma reached a finger's breadth into the duodenum, and in a 34 year old man to the papilla. On the other hand, a carcinoma of the cardia extends upward into the

FIG. 317.—Infiltrating and stenosing annular carcinoma of pyloric region (medullo-scirrhous form); massive infiltration of mucosa and submucosa; bulging of mucosa; penetration and partial atrophy of muscularis hypertrophic in the circular layer; gastric ectasia above; m, stomach; p, pylorus; d, duodenum; $\frac{3}{4}$ nat. size.

esophagus via the lymphatics, mostly in the submucosa, rarely in all layers, as strands or nodules or polypoid or diffuse growths.

Coexistent with carcinoma are other changes in the mucosa of the stomach, such as chronic interstitial gastritis, atrophy of gland epithelium, parenchymatous degeneration, etc., which go hand in hand with severe functional disturbances (for histology, see Matti). These are probably not secondary as a rule, but primary changes preceding the carcinoma (Matti, lit., Konjetzny, lit.).

The most remarkable change is the disturbance of the production of hydrochloric acid (p. 711).

According to Mayo in 54%, according to Anschutz-Konjetzny (lit.) at the most in 3 to 5%, in old calloused ulcers in 6 to 10%, carcinoma develops in the base or the margin of a simple ulcer, or in the scar of an ulcer (cylindrical cell, more frequently round cell, usually scirrhous) (Hauser, Haberlin, Verse and others). The atypical proliferations of epithelium mentioned on p. 687 are of importance because they may

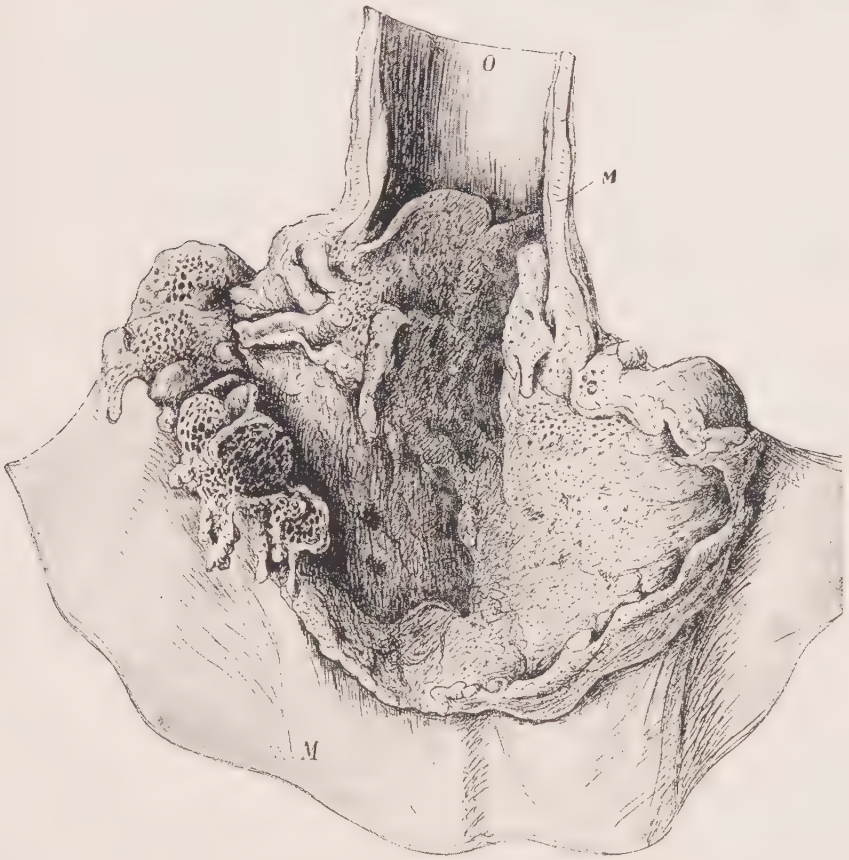



FIG. 318.—Ulcerating, stenosing carcinoma of the cardia extending to the esophagus, its margin thrown up, partly ragged and floating (adenocarcinoma); dilatation and hypertrophy of esophagus. M, stomach, O, esophagus with thickened circular muscle layer; ($M_1$), infiltrated submucosa; ¾ nat. size.

eventually change into carcinoma. This is seen in the small deep ulcers, their step-like descent still retained, especially those of the posterior wall, or in flat ulcers small or large, and finally in the almost linear flat u'cer scars. The author saw a carcinoma in a linear ulcer scar of the greater curvature, its bulk unimportant, produce a general nodular carcinomatosis of the peritoneum in a woman only 21 years old. Occasionally it can be demonstrated that a carcinoma springs from the edge, penetrates down-

ward, and infiltrates the base of the ulcer from below. Older villous thickenings are frequent in the serosa with adhesions to the surroundings and carcinomatous infiltration of the adhesions. Hirschfeld, on the basis of voluminous "statistics," denies any relation of ulcer to carcinoma, but Hauser has shown his error and the author from his own experience must contradict him (Gruber). Conversely, a peptic ulcer may develop in a carcinoma, especially those of slow growth (p. 687).

Metastases in adjacent lymph nodes are extraordinarily frequent; these are the epigastric (above the lesser curvature), portal, retroperitoneal, the more distant supraclavicular on both sides, more frequently the left (important diagnostically in occult gastric carcinoma!) nodes. This infiltration may be very large in comparison to the primary tumor; as for instance, in a 78 year old man, the author saw a small isolated carcinoma in the pyloric region and a mass of nodes the size of a fist around the cardia. It has been mentioned (p. 480) that the introduction of carcinoma cells into the thoracic duct distributes the growths especially into the lungs. The peritoneum frequently is markedly involved, the cells spread by continuity in lymph and tissue spaces, sometimes infiltrating the entire peritoneum in diffuse, brawny, cast-like growths or nodules and chains of nodules. Transudates, often sanguinous, collect in the abdomen (details under peritoneum). The liver is a very frequent site of metastases (according to the material in Basle in 33%), via the branches of the portal vein or retrograde in the lymph channels of the periportal connective tissue. As elsewhere, these metastases may be enormous while the primary tumor is quite minute (see under liver). This fact may lead to erroneous diagnoses in the living. At other times the carcinoma spreads in adhesions to the liver. Not rarely a gastric tumor continues to the hilum of the spleen or to its pedicle by way of the lymphatics. In both cases the spleen is more or less adherent to the stomach. Very rarely, a carcinomatous thrombosis from the stomach is implanted through the splenic vein into this organ (p. 246). Occasionally, metastases occur in many organs such as the lungs, both ovaries (see there), kidneys (rare), bones, the mammary gland, the skin not only of the abdomen but also, although rarely, of the arms and legs (Montier and Marre, lit.), by way of the blood circulation and retrograde extension through the lymphatics. In a 43 year old woman with carcinoma in an ulcer, the author saw the unusual metastasis in the musculature of the right thigh. See Witthauer in reference to umbilical metastases which are not rare.

In other rare cases numerous fungoid nummular metastases are found in the gastric mucosa and duodenum, or still lower down. These were formerly considered implantations although such a supposition meant little because the stomach has vigorous movements and its con-

tents are changing constantly and the gastric juice would probably soon destroy the cells before their implantation. The assumption of submucous dissemination within the innumerable lymph channels is more logical, the more so when the uppermost layers of mucosa are intact over the carcinomatous nodules and it is obvious macroscopically that the carcinoma developed from below, upwards. This appearance is not at all rare and is more frequent under the microscope.

The coincident appearance of a stenosing scirrhous (round cell) carcinoma of the pylorus and a stenosing carcinoma of the colon, the tumors histologically similar, is unusual but was seen by the author in a woman 39 years old. More often the histologies are different of a gastric carcinoma, and a second tumor of another organ. We have seen cylindrical cell carcinoma of the stomach with squamous cell carcinoma of the esophagus, and in a second case with a carcinoma of the os uteri. Examples of two primary carcinomas are seen in other places as well, *e.g.*, in the gall bladder and cervix uteri.

**Carcinoma of the Stomach and the Vomitus. Diagnosis.**—The vomitus in many gastric carcinomas contains disintegrated blood as demonstrated, *e.g.*, by the Techmann reaction modified by Hoppe-Seyler, *i.e.*, heating on a glass slide a small amount of the coffee ground vomitus after addition of glacial acetic acid and a few granules of NaCl. Dark brown hemin crystals form. This method (and others) also serves for the medico-legal demonstration of blood. Sometimes by good fortune, microscopic diagnosis is possible from tumor particles of a soft disintegrating carcinoma vomited or picked up by the stomach tube. Free hydrochloric acid is absent in the gastric juice in most carcinomas of the stomach (von den Velden); it is rarely absent in the healthy. Free hydrochloric acid can be demonstrated by the phloroglucin-vanillin test (Gunzberg), 2.0 gms. phloroglucin, 1.0 vanillin, 30 gms. absolute alcohol; mix a few drops with a few drops of gastric juice, heat in a porcelain dish over flame; at the border of the fluid a red edge appears. But the absence of hydrochloric acid is also observed in numerous other diseases of the stomach such as acute and chronic catarrhs, degeneration (p. 708), various cachexias, infectious diseases, etc. The frequent absence in gastric carcinoma is considered due chiefly to the accompanying diseases of the mucosa, chronic gastritis with atrophy of the specific gland cells. According to Matti, the carcinoma actually arises in such altered mucosae; indeed such changes are absent in only about 15% to 20% of the cases in which, as a rule, the carcinoma is derived from an ulcer. Therefore achylia is not pathognomonic of carcinoma, and as the author saw, cases are met with ulcer and carcinoma side by side and plenty of free hydrochloric acid. Nevertheless this finding is important when no definite

tumor can be felt in the epigastrium but there is a suspicion of carcinoma for some other reason such as cachexia, wasting, advanced age, vomiting, and other symptoms of stagnation, lactic acid fermentation, the presence of elongated lactic acid bacilli, possibly sanguinous vomiting, pain during digestion, palpable metastases, etc. (Rovsing).

Lactic acid, although not of specific importance (as believed by Sick, etc.) is nevertheless, present in considerable quantities in many gastric carcinomas especially of the pylorus (according to Strauss, in 70%; see Sandberg). But in spite of the absence of free hydrochloric acid and the presence of lactic acid, carcinoma may not be present. The author saw the following cases: 61 year old woman, dilatation of stomach, slight icterus, free hydrochloric acid absent, abundant lactic acid; diagnosis: malignant tumor of the pylorus; findings: very small scirrhous carcinoma of the gall bladder with adhesions and kinking of the duodenum; 32 year old man, pyloric stenosis due to ulcer, plenty of lactic acid, absence of free hydrochloric acid. Luger and Neuberger consider the presence of many spirochetae of the type of buccal spirochetae diagnostically important in gastric carcinoma. Many cases of carcinoma of the stomach are never recognized during life, notwithstanding exploratory laparotomy, *e.g.*, in a 45 year old man, a small, non-stenosing, ulcerating carcinoma of the cardia was completely covered by the liver which was much enlarged and filled with numerous soft metastases. The author has seen many analogous cases.

**Secondary Carcinoma of the Stomach.**— Secondary carcinomas occur most frequently by continuity from the esophagus and are of the squamous cell type.

The mode of spread is via the submucous, the subserous lymphatics, or both; in the first case tumors are concentrated in the mucosa. Many cases must be regarded as having spread in this way from the pharynx or esophagus rather than as transplantations on the gastric mucosa from autoimplantation of detached fragments (Klebs). See remarks in reference to so-called "implantation metastases," p. 710.

The rare metastatic carcinomas from distant places such as the breast, rectum, bronchi, etc., are implanted first in the wall of the stomach from which they grow into the mucosa, but the same conditions occur in primary carcinoma arising from a displaced submucous or subepithelial nucleus; they appear as flattened globular or nummular tumors sometimes with central depressions, or as hard infiltrated folds, or as larger plane surfaces.

### Degenerative Changes

Fatty degeneration of the glandular epithelium is caused by various hematogenous conditions. The mucosa is pale, opaque, milky; when the

fatty changes are advanced, it is yellowish white, and sometimes remarkably "geographic."

It is observed in febrile infectious diseases (parenchymatous gastritis) such as sepsis, typhoid fever, pulmonary phthisis, in which latter it may be combined with inflammatory infiltration and proliferation of connective tissue, in grave anemias, especially pernicious anemia (disputed by Herzberg, see p. 668) in which, according to v. Hansemann, purely glandular disappearance also takes place (anadeny) with atrophy of the submucosa and muscularis.

For the histology of the intestine in pernicious anemia, see Schlaepfer (lit.) and Herzberg 1 c., p. 668. It also occurs in chronic lead, arsenic and phosphorus poisonings (for histology see Blatter, lit.). It often accompanies chronic catarrh (especially in drinkers).

(Phosphorus produces fatty degeneration of the heart, liver, kidneys and other organs, so that the condition in the stomach is not a local result of contact but the effect of a general hematogenous action; it occurs also when phosphorus is introduced subcutaneously as in animal experiments.)

Microscopy. It is usually preceded by cloudy swelling and is found chiefly in the peptic glands; the mucosa is pale gray, opaque, succulent and creamy. Fatty metamorphosis may be added, but it is not a necessary sequence of cloudy swelling. In the diagnosis of cloudy swelling, care must be exercised not to mistake the normal cloudiness of the gastric glands from an accumulation of protein granules during the height of digestion; the chief weight should be laid upon the swelling and enlargement. O. Israel points out that the former cloudiness is confined to the middle and deeper parts of the glands, while in cloudy swelling the upper parts are also cloudy and swollen, inclusive of the surface epithelium; the gland margins project above the surface. The granules of cloudy swelling disappear as do the others on addition of acetic acid or dilute potassium hydroxide but these solutions do not affect fat granules. In unstained preparations (frozen section, etc.) the fatty glands appear silver gray to black with low power; with high power it can be seen that the gland cells and ducts are completely filled with fat granules and droplets. In pronounced cases, the glandular architecture becomes quite indistinct and the gland epithelium is partly desquamated.

(*b*) Amyloid is deposited in the connective tissue and blood vessels of the stomach in general amyloidosis, and has been known to cause dangerous hemorrhages, but this is not frequent. In still rarer cases, it is deposited in the stomach alone (Beckert, lit.).

### Stenosis and Dilatation of the Stomach. Volvulus

General narrowness of the stomach develops when the gastric function is more or less suspended, as in esophageal stenosis, refusal of food (in

insane), etc.; the stomach may be markedly narrowed by diffuse scirrhous carcinoma and also by chronic gastritis.

Partial narrowing is due to scars of peptic ulcers, more rarely to the scars of corrosions, constricting carcinomas, etc.; according to the location at the pylorus, cardia or the lesser curvature, there develop dilatation, narrowing, shortening, hour glass deformities, etc.

The so-called "benign pyloric stenosis" is of special importance; the various conditions are summarized below (Chiari).

1. Benign hypertrophy of the pylorus (Cruveilhier), plastic linitis—s. cirrhosis ventriculi (Brinton), sclerostenosis (Krompecher), benign, inflammatory, connective tissue muscle hypertrophy of the pylorus (Koch), consult pp. 667 and 668.

2. Congenital stenosis of the mucous channel with or without hypertrophy of the muscle (Landerer a. Maier); p. 652.

3. Hypertrophic stenosis of the pylorus and pylorospasm in infants (Hirschsprung); p. 660. This form may persist in adults.

According to Clairmont, many benign pyloric stenoses might be called "cicatricial stenoses" from active chronic duodenal ulcers. De Josselin de Jong also points out that annular, benign glandular proliferations around the pylorus may cause narrowing with its consequences.

General dilatation is due most frequently to the purely mechanical effect of a stenosis of the pylorus; in other cases it develops acutely from overloading and gastric paralysis. Sometimes there is primary chronic weakening of the wall, an atony of the musculature, induced by various pathologic changes of the mucosa and contents. Dilatation may reach such a degree that the stomach, relaxed and flaccid, reaches to the symphysis and completely covers the other viscera.

In a case of duodenal stenosis from carcinoma of the pancreas in a 32 year old man the stomach in situ in the dorsal position of the cadaver measured 37 cm. from above downward, 83 cm. along the greater curvature, 45 cm. horizontal circumference. Sometimes the esophagus, in other cases the duodenum, also (as in the above case), may participate in the dilatation; the pylorus becomes insufficient in the latter condition.

Mesenteric ileus, or arteriomesenteric intestinal occlusion is also remarkable (Kundrat, P. Albrecht, lit.), or as called by P. Albrecht, arteriomesenteric duodenal obstruction with gastric dilatation. The root of the mesentery containing the superior mesenteric artery is strapped down across the duodeno-jejunal junction; this causes non-fecal, but bile-containing vomiting. The obstruction can be felt by passing the finger from the jejunum into the duodenum; when the mesentery is lifted upward, the obstruction vanishes and the duodenal contents can pass into the jejunum. As soon as the mesentery is pulled firmly downward toward

the pelvis, the obstruction is reestablished. The dilated stomach may exert this pull by forcing the ileum downward and since the ileum may be dilated, it makes it difficult to recognize this type of obstruction; also if the ileum is empty and lies in the pelvis it probably pulls on the mesentery and cannot escape because of pressure from above. Whether forcing of the ileum downward by rapid filling with food difficult of digestion in a wide abdomen can exert sufficient pull (Wagner) is doubtful. But if the obstruction is once established, there is an acute increase in the gastric ectasia. The stomach may hold 8 to 10 liters of fluid. In addition to lavage, therapy consists of a lateral position, lying on the abdomen, elevation of pelvis, knee chest posture. Some clinicians assume there is primary acute gastric paralysis with subsequent arteriomesenteric ileus. O. v. Herff, Stieda, and others emphasize this primary acute gastric paralysis which may occur from chloroform anesthesia (usually after intraabdominal gynecological operation), or from direct mechanical trauma, especially inoperations on the biliary tract, or reflexly from the peritoneum by drainage, tamponade, etc. But while an acute gastric dilatation may cause arteriomesenteric ileus, it is not a necessary result; the dilatation may recover spontaneously. Albrecht mentions other less common causes, such as intense abdominal compression, acute fixation of the ileum in the pelvis from adhesions, etc. (lit. by Hopff, Neck, H. Albrecht, Kayser, Rosenthal, L. Landau, Borchardt, von Haberer, lit., Nakahara, Payer, lit., Kuru, v. Haberer, Huebschmann, Finsterer and others).

During life the cardiae of dilated stomachs are frequently opened by gases (belching, eructations) or gastric contents (vomiting). According to Kraus the rare cases of rumination occur from inspiratory aspiration of gastric contents into the esophagus, through an insufficient cardia (Jung). Pyloric stenosis is usually accompanied by functional muscular hypertrophy of the antrum which is the chief motor part of the stomach. This hypertrophy is able to compensate for minor degrees of stenosis, but in pronounced cases, the musculature becomes insufficient and degenerates (Kussmaul); this is followed by dilatation of the cavity, stagnation and abnormal decomposition of the gastric contents (compare with compensatory cardiac hypertrophy and stenosis of an opening).

Atonic dilatation without stenosis may also be caused by abnormal secretory processes in the mucosa. If but little hydrochloric acid is secreted (subacidity) and if much food liable to fermentation is ingested, the abnormal fermentation alone may cause dilatation, and finally atony. To this must be added that the proper acidity is absent and this is the most important stimulus to gastric peristalsis (as in chloroses and other anemias). Abnormal fermentation alone may cause atony (Quincke).

But dilatation without pyloric stenosis may also develop in cases of hyperacidity (combined with peptic ulcer?) and hypersecretion, if the empty stomach contains too much HCl. It is thought that the irritation of the acid produces pylorospasm.

In chronic gastric dilatation, the stomach contents are almost always sour and if the fluid is permitted to stand, fermentation occurs in many cases.

Microscopically the stomach contents disclose food remnants more or less unchanged, sarcinae ventriculi (ill. p. 561), yeast fungi, and bacteria of various types.

These fermentative processes develop under the influence of various microorganisms, especially yeast fungi, but also bacteria. Glucose may be changed to lactic acid, the latter to butyric acid, to H and $CO_2$, marsh gas ($CH_4$), and other combustible gases. If these gases are expelled they carry the acids upward from the stomach into the esophagus and mouth with the sensation of heart burn (pyrosis); in rare cases, rupture of the stomach may be caused by excessive formation of $CO_2$ by extreme fermentation (s. Verse, lit., see too Schencke, lit., in reference to gastric rupture due to internal factors).

Circumscribed dilatations or diverticuli are occasionally due to pull exerted by abdominal adhesions, peritonitic or peri-pancreatic and abdominal tumors. For diverticuli between ulcers, see p. 687. Sometimes heavy foreign bodies, for instance, coins, produce partial ectasia (lit. Handtmann, Nauwerck).

Gastric torsion or volvulus is rare; it occurs (*a*) around the mesenteric axis (the pyloric portion is turned upward toward the cardia while the fundus is bent backward); or (*b*) around the longitudinal axis (more rarely) forward or backward (v. Haberer). Ptosis, dilatation and particularly an hour glass deformity create a predisposition. In type (*a*) the pylorus and cardia twist around each other, each becoming occluded; in type (*b*) (hour glass stomach) only the pylorus is closed. The author first described (this textbook, 2nd edition, 1901) torsion of the stomach around its long axis due to a fibromyoma (p. 692); v. Haberer first described volvulus in gastric carcinoma. Type (*b*) is relatively frequent in diaphragmatic hernia, as described by the author in traumatic so-called diaphragmatic hernia. Lit. by A. Payer, Wilke, Reinecke, Richter (lit.), Th. Kocher, Siegel.

Acquired displacement is observed in hernias of the abdominal wall and umbilicus (*i.e.*, eventration) (lit. Tillmanns, Weber). [For chemical changes in the blood after pyloric obstruction, etc., see Haden, R. L. and Orr, T. G., J. Exp. Med., 37: 377: 1923.—*Translator.*]

### Foreign Bodies

In reference to various foreign bodies which are intentionally or accidentally swallowed (set of false teeth) or reach the stomach cavity during trauma, such as projectiles, consult the textbooks of surgery (Hochenegg). Among foreign bodies formed in the stomach, "bezoar" formation may be mentioned; it is very rare.

The term "bezoar" means antidote (counter-poison; the hair balls found in butchered animals were used in the Orient as remedies, *e.g.*, against epilepsy). Trichobezoars are masses of matted hair, hair tumors, or hair balls, as occasionally seen in the insane (lit. by Schopf and Meilchen). Phytobezoars are clumps of plant fibres. Hair and cotton fibres occur mixed (Purcacareanu). These formations which may weigh several pounds are often present in the stomach for years without producing reaction, but they may lead to hypertrophy of the gastric wall, cause ulcerative processes or become impacted in the bowel and cause perforative peritonitis. At times they pass completely through the bowel and are expelled through the anus. In animals (*e.g.*, the chamois) these bodies occur more frequently from licking themselves, or in the "wool chewing of sheep," or in dogs afflicted with rabies. Gallstones rarely reach the stomach. The drinking of alcoholic solutions of shellac produces shellac calculi or actual casts of the stomach (lit. Hallas). Literature in reference to foreign bodies of the gastrointestinal tract in man by Woelfler, Lieblein, De Josselin de Jonge. [For clinical, see Matas, R., Trans. South. Surg. & Gyn. Asso'cn., 1914.—*Translator.*]

## INTESTINES

**Anatomy.**—The layers of the intestine from within outward are: mucosa with muscularis mucosae, submucosa, muscularis (inner circular, outer longitudinal layer), subserosa and serosa.

The mucosa is covered by cylindrical epithelium. The glands are closely approximated tubes lined by cylindrical epithelium known as the glands of Lieberkuhn (crypts). In the cecum and appendix, the fundus of these glands contain the fuchsinophile cells of Paneth (Fischl, lit.), and throughout the whole intestine between the other epithelial cells are the so-called yellow cells of Schmidt (chromaffin with Muller formol fixation). Brunner's, or duodenal glands are submucous in the duodenum and empty into the crypts or intestinal lumen parallel to them. Their cylindrical cells resemble those of the pyloric glands.

Lymphoid tissue is distributed in the mucosa diffusely, and in circumscribed masses. The latter represent lymph follicles (lymph nodules).

elementary lymph nodes introduced in the lymph current, which, as pear shaped solitary follicles, are distributed throughout the entire intestine between mucosa and submucosa, and somewhat into both layers. They extend to just below the epithelium of the mucosa, while their larger, broader ends reach into the submucosa. The muscularis mucosae is absent over the follicles. They are larger in the colon than in the small bowel. Flemming found germinal centers in the follicles. Lymphocytes from the follicles pass through the epithelium to the surface and also into the lymph vessels. Peyer's patches, or agminated follicles, are oval groups of closely crowded follicles in the long axis of the bowel, chiefly in the lower ileum opposite the insertion of the mesentery, especially abundant around the ileocecal valve. The appendix is frequently lined with them. These plaques normally are but slightly raised, and are much more easily seen in children. Plasma cells and eosinophiles are abundant in the intestinal mucosa.

In the duodenum the mucosa has villi, between which are the outlets of the glands of Lieberkuhn. In the duodenum and jejunum (where Brunner's glands disappear, Helly), the mucosa has transverse folds (plicae conniventes, Kerkingii) which become less obvious as the intestine is examined lower down.

The outside of the colon has three longitudinal muscular bands, the taenia, to which correspond internal longitudinal bulgings of the mucosa. Transverse bulgings like the rungs of a ladder are found in the mucosa, between two taeniae, the semilunar folds. Each two semilunar folds and two longitudinal folds of the taeniae at right angles to the former, constitute a haustrum coli, a sacculation of the wall of the colon.

The peritoneal coat is incomplete in some parts of the intestine, viz., the descending part of the duodenum which is covered by peritoneum laterally, the ascending part of the duodenum which is covered anteriorly, the ascending and descending colon in their third portion directed toward the back and median line; the posterior middle part of the rectum and its lower portion are all completely free of serosa. The parts completely covered by peritoneum have a mesentery and are movable (jejuno-ileum, appendix, transverse colon, sigmoid flexure).

Lymph vessels, called chyle vessels, are very abundant. Each villus of the small bowel has a central chyle vessel enmeshed in a capillary network which ends blindly in the intestinal cavity, but externally passes into a capillary meshwork which is at the base of the gland ducts. From here the lymph vessels spread out in the submucosa, receive the efferent branches of a network between the two muscular layers, then pass through the subserous coat to the mesentery, and continue between its layers to the mesenteric lymph nodes.

Retention and congestion in the chylous vessels produce small chylous cysts in the mucosa and submucosa in the form of white dots and specks on villi and folds. The jejunum and duodenum are chiefly selected, and according to Leiulle, who calls them lymphatic varices, they are most frequent in chronic nephritis (Schujenioff).

Non-medullated nerves compose the myenteric plexus (Auerbach) lying between the circular and longitudinal muscular layers, and supplying the smooth muscle cells with motor fibres. Connected with this is the submucous plexus of Meissner. Both are equipped with numerous ganglion cells and lie in a sheath containing lymph, somewhat similar to a lymph node sinus (Gerota). These periganglionic lymph spaces must not be mistaken for ordinary lymph vessels. In most inflammations of the walls of the bowel, in typhoid fever, dysentery, and in peritonitis, these lymph sheaths are distended and thus especially clearly seen. (For anatomical details, etc., of intestinal innervation, see L. R. Muller.)

Blood Vessels. The superior and inferior mesenteric arteries enter the intestinal walls from without to be distributed in the submucosa from which they enter the mucosa. At the bases of the gland tubules and in the rest of the mucosa there is a wide capillary network emptying into the veins. (For anatomy, see Latarget and Forgeot, Descomps and de Labaudie.) The majority of the intestinal veins end at the portal vein.

**Measurements.**—At birth the small intestine is about 5 times as long as the baby itself, while the large bowel practically corresponds to the baby's length. In the adult, the large bowel corresponds also to about the length of the body (according to Curschmann, 142 cm.). All of the intestines are about 5½ times the body length (according to Gegenbaur, 5.5 to 6.5 m.). These measurements are subject to wide individual differences; *e.g.*, there are large bowels almost 3 m. in length and small bowels over 9 m. long. The author saw a large bowel 2.47 m. and the appendix 19.5 cm. in length. People who are essentially vegetarians are said to have especially long intestines (intestines of Russians, v. Hansemann, lit.). The intestinal contents stagnate in the cecum and sigmoid; the transverse colon usually has little or no contents.

Meconium: When the secretion of bile commences in the liver (about the 4th fetal month) it reaches the bowel, is absorbed by the epithelium and re-expelled into the bowel as oval structures—meconium bodies—(pp. 360 and 858). Since the fetus swallows amniotic fluid, desquamated skin, lanugo hairs, vernix caseosa, etc., are mixed with the meconium.

### Malformations of the Intestinal Tract

Total absence occurs only in most pronounced acardii; large defects occur only with other grave malformations. Small defects are not rare.

An abnormally short large intestine (120 cm.; 167 body length) was seen by the author in a 27 year old soldier. The place of the cecum was occupied by the end of the ileum which was attached there; the short cecum (the appendix retrocecal-retroperitoneal) was barely 8 cm. to the hepatic flexure. The appendix is rarely completely absent (Schridde, Miloslavich, lit.); the author saw 2 cases, one in the collection at Basel, the other in a 74 year old man. It may be abnormally small.

**Congenital Stenoses and Atresias.**— Narrowing (stenoses) or complete occlusion (atresia) is sometimes multiple in various sections of the bowel, as in the duodenum at the openings of the common duct and the duct of Wirsung, at the junction between ileum and cecum (ileo-cecal atresia), in the colon and most frequently in the hind gut (lit. in appendix).

The lumen is closed, or there is a complete interruption of the continuity, *i.e.*, a defect often combined with a defect of the mesentery. Atresias and stenoses are said to be due to (*a*) pathological changes in the nature of peritonitis or enteritis, or obstruction of mesenteric arteries, or axial torsions (doubtful, primary or as complication of narrowing due to malformation, see Leischner), or invaginations (lit. p. 744), or developmental anomalies (p. 719), such as anomalies of the vitelline duct (Kreuter, lit.) analogous to obstructions of the esophagus, due to primary absence or defective formation of the intestinal lumen (occlusion theory). During a certain time (30th to 40th days) in the embryo, the gut, at first hollow, becomes temporarily closed here and there by epithelial overgrowth (Tandler's embryonal atresias of the duodenum), to be reopened later (60th day). If these embryonal atresias persist partially or totally, they constitute congenital atresias or stenoses. Schridde opposed this conception, because he never found embryonal epithelial atresias, but Kreuter (lit.), supported by Forssner in all essential points, still maintains his conception. Recently Fanconi has cast doubts on the general occlusion theory (see Hauser, Odermatt, Kermauner, lit.). Above the narrow part, the lumen is enormously distended by swallowed amniotic fluid, and the muscularis becomes hypertrophic. Phlegmons, ulceration, and even perforation have resulted. The lower segment collapses, the wall atrophies, and the lumen is completely obliterated. A combination of duodenal atresia, defective formation of the esophagus and atresia of the rectum was seen by Marckwald, Mensburger (lit.).

Under the name of Hirschsprung's disease, various conditions, more frequent in boys, are considered. The continuous unyielding constipation and the distension of the abdomen from birth, are clinically uniform. The entire colon is dilated and hypertrophic, often enormously so, with the exception of the rectum; or the sigmoid flexure is affected especially. In an 11 months old child with its abdomen distended from birth, and the typical

symptoms of Hirschsprung's disease, the author saw dilatation beginning about 10 cm. above the anus, involving the sigmoid (11 cm. long) only moderately (3 finger's breadth), but all of the rest of the colon to the highest degree (circumference up to 28 cm.) with considerable thickening. The colon was 79 cm. long, the tenia libra were almost 2 finger's width wide; the appendix, also involved, was almost as broad as the little finger. A case in which the dilatation and hypertrophy were confined chiefly to the sigmoid is illustrated in fig. 319.

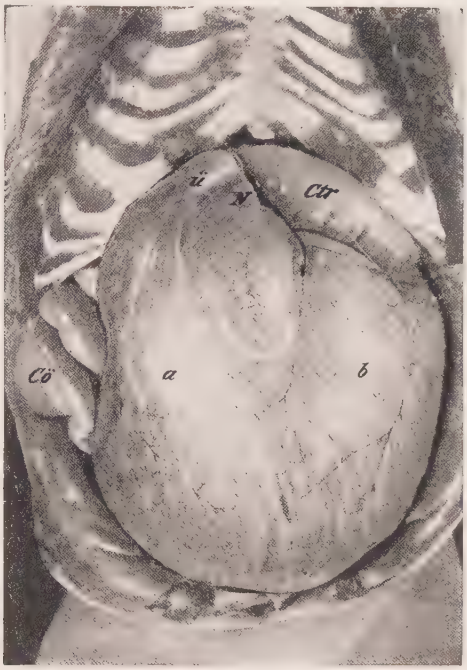



FIG. 319.—In Hirschsprung's disease; girl 11 months old; a, afferent; b, efferent limb of the bulging, enormously distended sigmoid; to a, also belongs a piece of desc. colon, which suddenly becomes narrow. Ctr, transv. colon; N, part of the hidden omentum; Co, cecum with inlet of ileum; above this, 2 loops of ileum; about ¼ nat. size.

The pathogenesis is divided into 2 groups:

1. Congenital origin (Hirschsprung and others). (*a*) Primary distension and hypertrophy of the colon as a malformation, "megacolon" or congenital "megacecum" (Mya, consult Haim); (*b*) unusual length and mobility of the sigmoid with the formation of loops and obstructions (Marfan, Ibrahim, Perthes, and others) or pressures of one loop on another (Bessel-Hagen), thereby (even in utero) producing hypertrophy and dilatation of the colon. In a 5 weeks old boy, the author was able to demonstrate a valve-like kinking of the sigmoid against the rectum (s. I Diss. R. Pfitzerer); the same occurred in an 8 weeks old boy and in a man

44 years old (P.M. 99) with symptoms of ileus and advanced marasmus (Goppert, Wieland, de Josselin de Jong, de Jong and Muskens and de Jong and Plantenga). As chief factors, Heller and Konjetzny stress the position and shape of the fetal mesosigmoid which may also cause torsion and volvulus. Likewise, an abnormally large rectal valve of Houston may constitute an impediment to the passage of contents (Goebell, lit.). This cause is logical to the author in the case illustrated, fig. 319, in which a high transverse fold, 5 cm. above the anus, formed the lower end of the dilated sigmoid. The dilatation extended to where the lifted descending colon, behind the pear-shaped sac, suddenly became narrow; there was general, relatively moderate, dilatation above.

According to Goebel, a megasigmoid is the most frequent cause of deep colonic invagination in children.

2. Acquired through mechanical impediments, such as torsion, spastic contraction (Fenwick). Cases acquired later, such as constriction from adhesions (Hoffmann), or after dysentery (Steiner), are not Hirschprung's disease (Goebel). (Lit. by Loewenstein, Danziger, Petrivalsky, Puls, Zoepffel, Kleinschmidt, Neugebauer, Schneiderhohn, and others.) [Bartle, H. J., Am. J. M. Sci., 171: 67: 1926.—*Translator.*]

The most frequent, and the most important form of congenital atresia, from the practical viewpoint, is ano-rectal atresia.

Short summary of the development of the normal anus: at first there is a cloaca communicating with the genito-urinary tract and the hind gut. It is closed externally by the cloacal membrane which is composed of an endodermal (inner) and an ectodermal (outer) layer; the membrane also closes the endodermal cloaca. The layers of the membrane are at first in close approximation to each other (fig. 289 I), but later at only one small place, because mesodermal tissue pushes in between the layers (fig. II). In this small area the external genitalia are developed and the two lateral margins of the cloacal membrane become elevated into folds (genital folds) which connect cranially with the developing genital tubercle (fig. II and III and fig. 604), while posteriorly the caudal stump projects, *i.e.*, the part into which the last portion of the posterior or end gut reached, to become rudimentary (the epithelial remnants are suggested in E. R. in fig. II). These parts now surround an open pit, the so-called ectodermal cloaca, or better called congenital pit after Stieda, whose description is followed closely; its base is the cloacal membrane (fig. III). But at the same time, an internal separation occurs, when the upper wall of the cloaca descends as a fold from above, followed by the peritoneum, which divides it into a ventral (bladder) and a dorsal (rectum) portion. But a gap remains at first between this fold and the cloacal membrane which makes communication possible between the ventral and dorsal

tubular organs (fig. III), which is very important in reference to developmental anomalies to be mentioned (sub. II). It soon reaches the cloacal membrane, and, with a mass of mesenchyme growing upward from the cloacal membrane (urorectal septum), it completes the separation into rectum and uro-genitalia. Where the septum reaches the ectodermal layer of the cloacal membrane, is the primitive perineum (P. D. in fig. IV). In this way the cloacal membrane is divided into two portions, one closing the urogenital cleft called urogenital membrane (U. G. M. in fig. IV) while the other, the anal membrane (A. M.) closes the rectum. Both close the so-called ectodermal cloaca. This shallow very rudimentary pit becomes divided into a urogenital furrow and an anal furrow as the perineum develops further by growth of the frontal partition.

The genital furrow, surrounded by the genital folds, then develops further; the genital tubercle becomes the clitoris or penis, the urogenital membrane disappears and the urogenital sinus opens into the genital furrow. The anal membrane disappears later, but it must be remembered that, according to Keibel, whose investigations are thorough, the anus is not situated at the place of rupture of the anal membrane, because with the voluminous development of the true perineum, and the further growth of the frontal partition, the anal membrane is placed in the depths of the ectodermal anal pit (comp. figs. IV and VI).

The most important changes to be considered are:

**Simple Congenital Anal and Rectal Atresia.**—(*a*) Simple anal atresia (fig. V). The rectum ends blindly at the external skin; no anal opening is present.

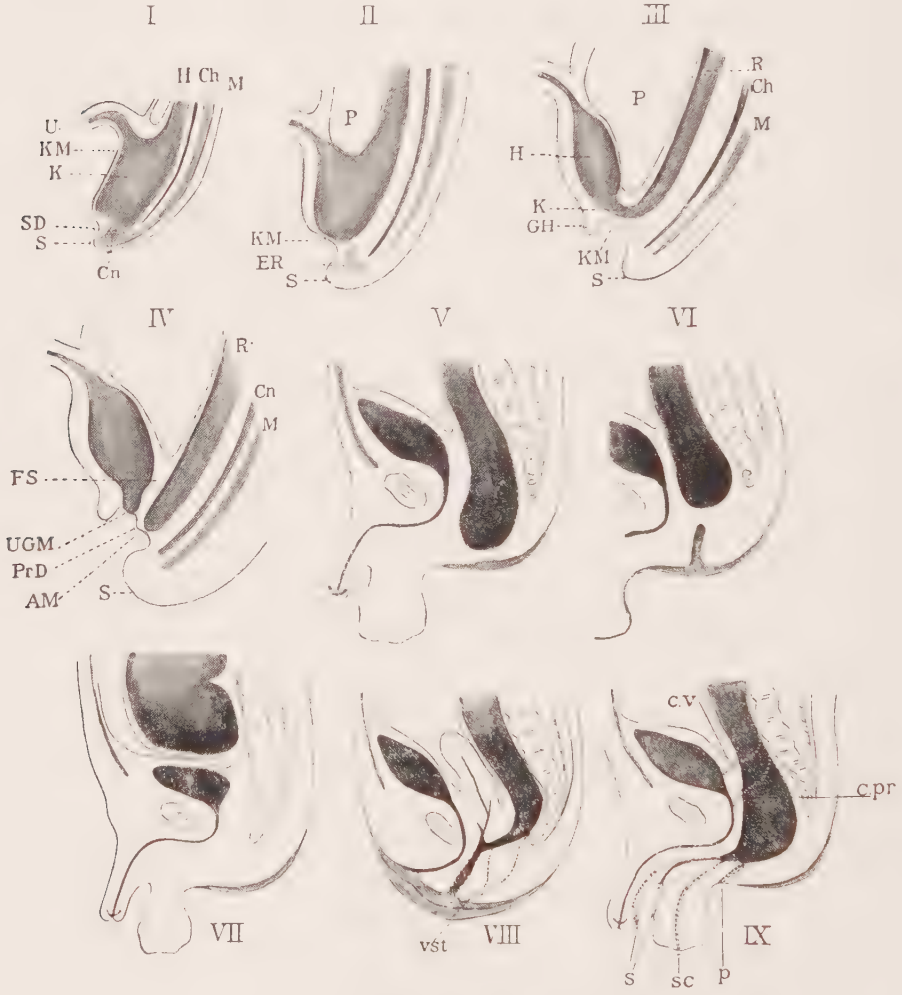
(*b*) Simple rectal atresia (fig. VI). The anal opening is present, but it leads into a short cul de sac (anal pit). The blindly ending colon reaches the blind end of the rectum.

(*c*) Anal and rectal atresia (fig. VII). The rectum ends blindly high above; the anal pit is absent. There is a greater or less distance between the blind end of the rectum and the outer skin.

The explanation of (*a*) and (*b*) is obvious. (*c*) is more difficult to explain since the rectum never ends so high up in any developmental stage; for this reason it must be assumed that there is a progressive atrophy of the hind gut, or that after separation of the bladder and rectum the caudal end of the rectum becomes detached from the cloacal membrane by the proliferating mesenchyme in a sort of snaring off action (Keibel, Stieda).

II. Absence of anus and communication of rectum with urinary bladder or urethra in the male, and with the vagina in the female. This union was formerly, and even today, designated as an internal fistula (v. Esmarch) (Frank, and others). Stieda suggests the name "communi-

cation" and differentiates anal atresia (or rectal) complicated with communications.




FIGS. 320–336.—Diagrammatic after Stieda (I–IV) and v. Esmarch (V–IX). I–IV. Development of urogenitals and rectum from the cloaca stage. U, urachus in allantoic pedicle; K, cloaca; KM, membrane of cloaca; SD, caudal gut; Cn, neurenteric canal; H, hind or end gut; Ch, chorda; M, medullary tube. Fig. II; P, peritoneal cavity; ER, epithelial rests of caudal gut. Fig. III; H, urinary bladder; R, rectum, GH, genital tubercle. Fig. IV; FS, frontal dividing wall; UGM, genito-urinary membrane; PrD, primitive perineum; AM, anal membrane. V. Atresia of anus, simple. VI. Atresia of rectum, simple. VII. Atresia of anus and rectum. VIII. Ano-vaginal atresia; atresia of anus and communication of rectum and vagina; punctation gives anal atresia with vestibular fistula. IX. Dual atresia with suburethral fistula (s), scrotal (sc) perineal (p) and indicating anal atresia and communication of rectum with bladder (cv) and with prostatic area (c.pr).

(*a*) Atresia ani vaginalis: anal atresia with recto-vaginal communication (fig. VIII).

(*b*) Atresia ani vesicalis: anal atresia with rectovesical communication (fig. IX).

(*c*) Atresia ani prostatica: anal atresia with communication between the rectum and the prostatic part of the urethra (C Pr. in fig. IX).

Fig. III gives the explanations in terms of developmental interference; the parts remain at an earlier developmental stage with retention of communications between the rectum and neighboring cavities, or channels. If the anal portion of the rectum communicates with the vagina, this can be explained, according to Stieda, only by a disturbance of the anlage of the primitive perineum. It may also be mentioned that rare cases of anal atresia occur in which a real cloaca persists into which both the bladder and rectum empty.

III. Anal (rectal) atresia with fistulae. The fistulae empty in the median line of the body surface. This is spoken of as external fistula and there are differentiated:

(*a*) Anal atresia with perineal fistula (indicated in fig. IX) in the perineal raphe.

(*b*) Anal atresia with scrotal fistula (fig. IX) in the scrotal raphe.

(*c*) Anal atresia with suburethral fistula (fig. IX) in the raphe of the penis.

(*d*) Anal atresia with vestibular fistula (fig. VIII v.s.t.) in the vestibulum of the vagina.

Explanation: These are not fetal malformations, but results of pathological processes; the pressure of meconium causes the pathological rupture. The wall of the fistula is partly without epithelium, and cicatricial (Stieda). For this reason alone, Frank's explanation is incorrect that external fistulae (which he separates from internal fistulae) were connected with Reichel's furrow, which lies completely within the ectodermal area, the closing line of which is situated on the epidermal surface, as emphasized by Keibel and Stieda; consult Sternberg, Kermauner, and the interesting new statements in reference to the development of the caudal sections of the bowel and the urogenital system of man on teratological bases, by v. Berendorf-Gosslen, (lit.).

**Congenital or True Diverticulae** (see p. 749).—Meckel's diverticulum, so-called, is found rather frequently as a blind ending protrusion of the ileum with which it communicates by a wide mouth; apart from its muscularis, which is at times somewhat thin, its structure is analogous to that of the bowel wall (true diverticulum); it is located opposite the mesenteric attachment, in adults about 1 m. above the ileo-cecal valve. In the newborn it is about 0.3 to 0.5 m. above the valve. It is usually the size of a finger, but may be longer and wider. Sometimes the diverticulum has its own mesenteric attachment with vessels from the omphalomesenteric

vessels. The end of the diverticulum may be split or lobulated. It is a remnant of the omphalomesenteric duct and constitutes the most frequent congenital anomaly of the intestinal tract.

The diverticulum may contain islands of gastric mucosa; in rare cases, it may even be lined throughout by gastric mucosa (Huebschmann, lit.). It is occasionally combined with other congenital anomalies; the author saw it with mobile cecum, aberrant pancreas, etc. Its length varies between 3 and 30 cm., the diameter 1.25 to 5 cm. Its point of departure from the bowel in adults may be ½ to 1 m. or at most 2 m. above the ileocecal valve.

According to Hilgenreiner and Fehre, a diverticulum is found in every 54 or 50 cadavers, figures verified by the author in 300 cadavers in Gottingen. Doepfner (lit.) found 1 Meckel's diverticulum in 65 bodies.

The omphalomesenteric duct, vitello-intestinal duct, yolk stalk (accompanied by the omphalomesenteric vessels) communicates in the embryo through the open abdomen with the yolk sac in the embryonic membranes. When the abdomen closes (umbilicus) the duct is obliterated; should its proximal part remain open, it becomes a Meckel's diverticulum which develops like a part of the ileum.

In the most severe cases, the abdomen remains open below the umbilicus, and the ileum opens in this situation, while the lower parts of the bowel remain empty. When a small opening persists in the umbilicus, while the lower portion of the bowel acts as a passageway for contents, it is an omphaloenteric fistula. An open Meckel's diverticulum is one which opens into the umbilicus (prolapse of diverticulum, described below).

Sometimes the end next to the bowel remains open while the obliterated end leads to the umbilicus as a cord. This may cause obstruction from entanglement of loops of intestines.

Such cords are important when the omphalomesenteric vessels, leaving the mesentery, are inserted at the distal end of Meckel's diverticulum or close by, or even into the umbilicus. In the first case, a closed snare is formed in which intestinal loops may become incarcerated (E. Neumann).

Diverticulum prolapse (Kustner) is an eversion of the diverticulum mucosa around the umbilicus (Kermauner). Macroscopically this may be mistaken for the velvety, bright red granulations, as large as a pea, of umbilical granulomas (see under skin). From snared off remnants of the duct, the so-called embryonal umbilical adenomas may arise which are small, bright red, velvety, sometimes polyp-like pedunculated tumors. (Lit. by Mintz, Ehrlich, Horzenberg, Waezeler, Zitronblatt, Lindau, Mathias, who speaks of choristoplastomas). Barron (lit.) emphasizes that even if these contain gastric mucosa, and not bowel mucosa, in some cases, they are not necessarily gastric diverticuli, but the glandular char-

acter probably depends on the time when the snaring off process took place. Carcinomas may originate from these structures (lit. by Bruggemann, Mariani, Kirschner), and may be mistaken for metastases of carcinomas hidden elsewhere (Quenu and Lonquet, etc.).

If a Meckel's diverticulum becomes closed to the bowel (often merely by a fold of mucosa), the accumulated secretion may produce a large sac filled with fluid, usually situated in the abdomen, more rarely in the umbilicus, and called a yolk duct cyst, or an enterocystoma (Roth). Recognition becomes difficult if there is no connection, not even a cord, with the bowel. The structure of the wall is analogous to that of the intestinal wall, but sometimes its epithelium has cilia (Roth). They are serious when the pedicle becomes twisted and the cystoma is gangrenous; lit. by Colmers, Niosi, Leuss. According to Roth, enterocystomas may also arise from a supernumerary bowel belonging to a rudimentary twin, or by closure of the gut begun normally; Hedinger believes mesenteric cysts may be snared off portions of esophagus, and therefore should be classified as intestinal cysts. Apart from these larger sacs, there occur smaller projecting intestinal cysts, developed from the remnants of irregularly closed ducts (Gfeller, lit.), although Kostlivy considers it more probable that multiple cysts develop from true congenital intestinal diverticuli. Enterocystomas are rare and are almost always found in young individuals, mostly children (lit. by Runkel and Roegner, K. Meyer). Schmincke described a rare intramesenteric and intrathoracic enterocystoma (good lit. and summary); v. Both described an umbilical hernia containing a Meckel's diverticulum. If a Meckel's diverticulum becomes fixed at any place of the peritoneum, it may entangle and incarcerate a loop of intestines; the diverticulum may become necrotic (Deus). Kinking of the bowel by pull or axis torsion (Hilgenreiner, lit.) is less frequent. The free Meckel's diverticulum may constrict loops including mesentery by forming an actual knot. This volvulus of the diverticulum may cause its gangrene (Monti; p. 748). Inversion into the bowel lumen, intussusception, is very rare; it may lead to intestinal invagination and cause death (Ewald, Kuttner, Kothe, lit.); gangrene and perforation have been observed (Denecke, lit.).

**Translator's Remarks.**—Meckel's diverticuli when treated surgically should be removed and not inverted and sewn over. The translator has seen two cases of intussusception follow the latter procedure.

Inflammations of Meckel's diverticulum, diverticulitis, are clinically similar to appendicitis (Rebentisch, Hilgenreiner, lit.), as are the rare protrusions with prolapse of open Meckel's diverticuli (Zondek, lit.,

Finsterer). See Pabst (lit.), Harf, Budde, in reference to inflammation and incarceration of Meckel's diverticulum in hernial sacs. Tuberculous and typhoid ulcers (rare, Morel) have been seen in Meckel's diverticuli; some have perforated (lit. by Stern). P. Muller (see Huebschmann) reported perforating peptic ulcer. Foreign bodies have also been observed in Meckel's diverticuli (lit. by Borggreve).

Meckel's diverticulum may contain an aberrant pancreas the size of a lentil or pea (H. Albrecht and Arzt); it may even be found in the umbilicus. These must not be mistaken for cases in which the diverticulum is caused by the pull of an aberrant pancreas, and is not a Meckel's diverticulum (Neumann, Nauwerck). Tumors are very rare. The collection of Basel contains a spindle cell sarcoma of Meckel's diverticulum, found in a woman 72 years old. This is the first case of that sort (see sarcomas by Tschiknawerow with perforation, lit. Hassner, Hedren). Button-shaped myomas have been reported.

Hernia-like bulgings of inner layers through congenital gaps in the muscularis have been held responsible for spontaneous intestinal rupture in fetuses and the newborn (Rudnew, lit.). Other congenital intestinal diverticuli are quite rare, (Glaus); consult under appendix.

One of the greatest of rarities is duplication of single loops of the ileum, and still more rare, of the colon. Other malformations are usually coexistent. Moller (lit.) described a double hind gut, Laewen, duplication of the cecum and appendix; the author saw duplication of the appendix (lit. by v. Berenberg-Gossler).

### Changes of Position

**Congenital Changes of Position.**— There occurs reversal of parts, as in a mirror, called transposition of viscera, as a part of a general inversion, or of the abdominal organs alone, or of some abdominal organs (lit. by Risel, Hart, Marchand, v. Werdt and lit. p. 96). It usually involves all the viscera (Lochte). Of the several parts, the colon, especially the cecum, may be abnormally situated, *e.g.*, when the colon is too short, it may lie in the umbilical region or higher. If the cecum has an independent mesentery, it becomes abnormally mobile (mobile cecum). If a larger or smaller segment of the colon has a common mesentery with the ileum, there is a tendency to axial torsion around the mesenteric axis, finally of all intestinal loops. For the importance of a common mesentery in kinking and dilatation (as in Hirschsprung's disease), see Goebel. At times the whole colon lies to the left, and the ascending colon in the splenic area becomes immediately the descending colon.

**Hernias (Ruptures).**—A true hernia or rupture is a displacement of an abdominal viscus into a peritoneal pouch.

If the abdominal organs escape without being surrounded by a peritoneal sac, the condition is called prolapse.

The word hernia is used in a wider sense when an organ, or portion of one, passes from a cavity through an opening, or into another cavity, *e.g.*, the stomach through a diaphragmatic tear into the pleural cavity without being surrounded by the diaphragmatic peritoneum, but in such cases, it is better to speak of ectopy.

If, (Honnerbach, lit.), an intestinal loop should pass through and be incarcerated in an abdominal gun-shot wound, it also is spoken of as a hernia, although the peritoneal sac is absent.

True hernias pass through congenital or acquired clefts (external hernias) and appear under the skin (with the exception of an obturator hernia), or abdominal viscera enveloped in peritoneum pass into the thoracic cavity, or abdominal viscera are displaced within the abdominal cavity itself into peritoneal pockets (internal hernias).

Hernias develop (1) by the passage of an abdominal viscus into an already existing sacculation, or (2) the peritoneum is gradually forced outward by the intraabdominal pressure at some point more yielding, weaker in structure, and less protected by muscle (hernias are more frequent in the hard working classes); or (3) suddenly from excessive force, as in trauma; or (4) by external pull sacculating the peritoneum from the outside and creating a suitable path for a viscus. This latter mechanism operates in some femoral hernias. The most important hernias occur in the congenitally weak places in the abdominal wall, where vessels, nerves and canals leave the abdominal cavity.

External hernias are the more important. The following factors should be considered:

The hernial sac consisting of the peritoneal pouch and the subserous tissue (peritoneal fascia) is forced outward through some opening in the soft parts; the neck of the sac is in the opening, where the peritoneum is arranged in longitudinal folds (fig. 339). When the pear-shaped sac is filled, as, *e.g.*, by a loop of intestine, the hernia is complete. The contents slip back, or remain, or pass in and out. Thus the sac is quickly or gradually dilated and the hernia becomes larger. As the sac advances, it displaces the adjacent connective tissue which becomes an accessory covering (fascia propria) of varying thickness depending on the hernia.

The contents of a hernia consist: (1) of omentum or intestinal loops, at times, the appendix or mesoappendix (v. Bruns), or (2) of organs, such as the ovary (lit. Heegaard), spleen, gall bladder, uterus (very rare, see Schulze), even the pregnant uterus (v. Winckel), tubal pregnancy (Jordan), accessory tube (Penkert), etc., or (3) of a portion of organs such as the liver, stomach (Maag, lit.; Ahrens), the ureter (Carli, lit.), diverticulum

of the urinary bladder (Konig). In male pseudohermaphrodites, a uterus and tubes were found in hernias (lit. by Hilgenreiner). It also consists of a small amount of fluid, derived from the serosa.

Tumor masses may be established in a hernial sac, *e.g.*, carcinoma of the ovary. It may also participate in a general tuberculous peritonitis which may cause considerable increase in the hernial fluid.

The mobile ileum is the organ found most frequently in hernias, but in larger examples almost the whole of the small bowel and part of the colon may enter. Small hernias usually contain parts of organs. A small portion of intestinal wall alone in a hernia is called a Littre's hernia.

If the hernial contents can pass in and out freely, it is called reducible. In an irreducible hernia, the contents remain in the sac because they are held by adhesions, especially frequent around the opening, or because they are firmly constricted by the elastic neck, or because they swell and become more voluminous within the sac.

### The Individual Forms of Hernia. A. External Hernias

**Inguinal Hernia.**—When the stretched anterior abdominal wall is viewed from behind (figs. 337 and 338), in the midline is disclosed the

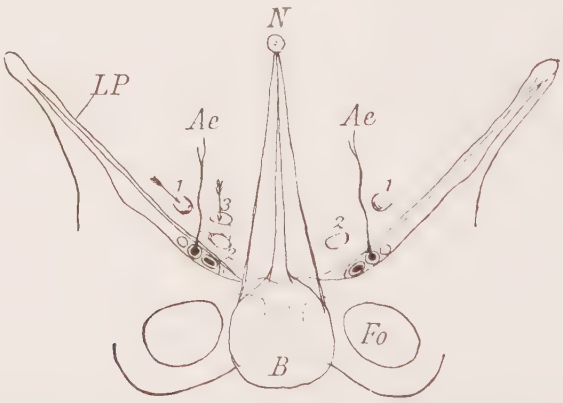



FIG. 337.—Diagrammatic presentation of anterior abdominal wall and pelvis (posterior aspect as in fig. 338). B, bladder connected with umbilicus by median vesico-umbilical and lateral vesico-umbilical ligaments; LP, Poupart's ligament (inguinal); below this from within outward: vein next to Gimbernat's lig; artery from which ascends the inferior epigastric (Ae) and the femoral nerve; 1, internal ring of inguinal canal; 2, external ring; 3, internal orifice of direct inguinal hernia; Fo, obturator foramen.

median vesico-umbilical ligament or median umbilical plica, the former urachus connecting the urinary bladder and allantois; externally, on either side is a small pit, the internal inguinal fossa, which is bounded externally by the lateral umbilical ligament containing the obliterated umbilical artery. External again is the outer inguinal fossa, which is divided into an inner and outer portion, the median and outer inguinal fossae, by the

peritoneal elevation over the epigastric artery (fig. 337). (Excellent illustrations by Enderlen-Gasser. Stereoscopic pictures for the study of hernias, Fischer, Jena, 1906.)

**External or Indirect Oblique Lateral Inguinal Hernia.**—The passageway of the spermatic cord is located in the outer inguinal fossa above Poupart's ligament, where there was previously a peritoneal pouch, the inguinal canal, formed by the descent of the testicle. Later this canal is usually almost obliterated and closed toward the abdominal side (see below); but if it remains open, and a peritoneal sac is formed, it constitutes congenital external inguinal hernia.

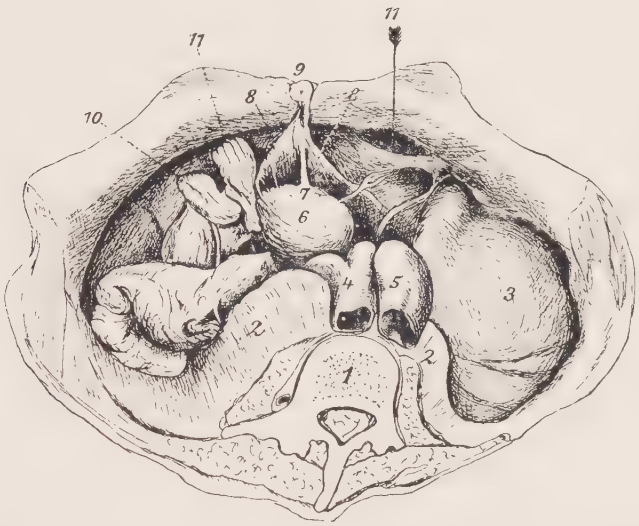



FIG. 338.—View of pelvic cavity with two femoral and two direct inguinal hernias; to right, without, left with contents of hernia; drawn from Atlas of Rudinger (plate III, fig. C). 1, vertebral column and bilateral psoas muscles; 2, peritoneum and fascia; 3, iliac fossa with peritoneal covering; 4, abdominal aorta; 5, inferior vena cava; 6, urinary bladder, much contracted; 7, median vesico-umbilical lig; 8, lateral vesico-umbilical ligs.; 9, umbilicus; 10, inner opening of crural hernia; to left with contents; 11, inner hernial opening of direct inguinal hernia, leading directly from behind forward.

The hernial sac is thus nothing but the open vaginal process, the peritoneal projection due to the traction of Hunter's gubernaculum which pulls the testis with its peritoneal covering from the abdominal cavity through the inguinal canal into the scrotum. The vaginal process closes from the inguinal canal to the testis after birth, remaining open only on the testicle and part of the epididymis (cavum scroti). The serous membrane is the duplication known as the true tunica vaginalis of the testis. Testis and spermatic cord are surrounded by the common tunica vaginalis which corresponds to the transverse abdominal fascia under the peritoneum, also pulled downward (fig. 340). If the vaginal process remains completely open, the hernial contents occupy part of the same space as the testis.

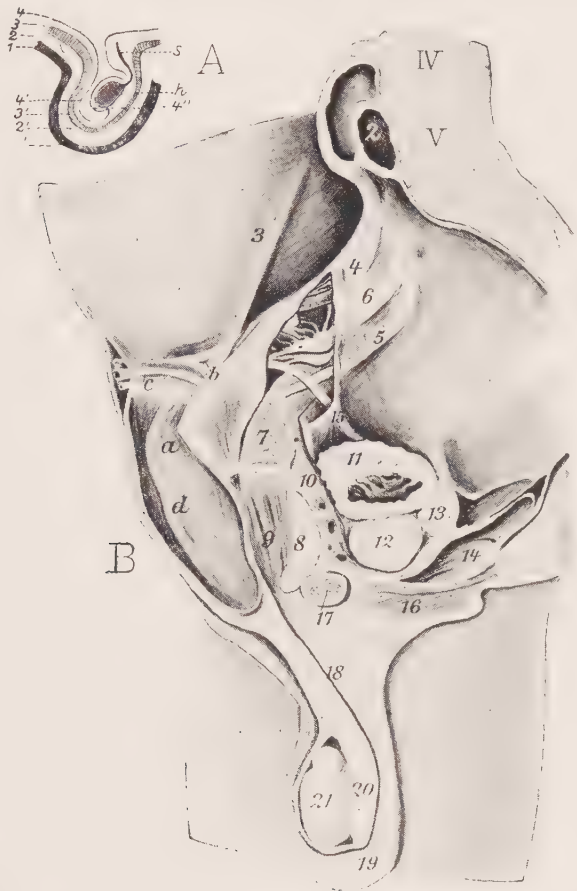
The opening facing the abdominal cavity, which gives passage to the spermatic cord, is called the internal ring; the outer opening from which the spermatic cord emerges between the abdominal coats, is the external inguinal ring. An external inguinal hernia follows the path of the spermatic cord; it passes through the internal ring into the inguinal canal, traverses an oblique direction through the canal and escapes through the external ring (indirect, external, oblique inguinal hernia). The oblique course, however, is well seen only in small hernias. Large indirect hernias with wide necks have direct paths from front to back (like internal inguinal hernias). While the larger proportion of external inguinal hernias are congenital (Hansen), others are acquired by a new outpouching of the peritoneum, into and through the inguinal canal, even as far as the scrotum. The hernial contents are always separated from the testis (fig. 339).

FIG. 339.—Inguinal hernia, with slight hydrocele; perpendicular section after hardening in chromic acid. H, testicle and epididymis; a, hydrocele; b, neck of hernial sack; c, spermatic cord.

**Internal or Direct or Straight Inguinal Hernia.**—When the index finger of the right hand is pushed with some force directly forward into the left median inguinal fossa (best on a thin cadaver of an older individual), the peritoneum is pressed into the external inguinal ring, and if this is open and the peritoneum will stretch, it is pushed outward as a sac; a direct inguinal hernia takes this route (fig. 340), *i.e.*, from behind forward through the abdominal wall; this occurs only if the parts give way. If a small external inguinal hernia is present and a finger of the left hand is passed obliquely downward and inward through the inguinal canal, the finger will touch the right index finger covered by peritoneum at an acute angle in the external inguinal ring; in other words, an external and an internal inguinal hernia cross each other (fig. 337). If the deep epigastric artery (fig. 340) is used as a guide, all external to it is called "external," or indirect, all internal is called "internal" or direct, inguinal hernia. The rare hernias of the internal inguinal fossa, which lies between the median and the lateral umbilical ligaments, are not considered in this discussion.

In both the acquired external and internal inguinal hernia, the hernia itself must push out the peritoneum. The congenital (external) inguina

hernia finds a sac already prepared. Direct inguinal hernias usually occur in older, lean individuals and develop gradually as the lower part of the abdominal musculature becomes thin and weak. A plug of fat may help in




FIGS. 340 and 341.—Testicle in scrotum; its sheaths: 1, abdominal skin; 1-1, scrotum with dartos layer; 2, superficial abdominal fascia; 2-1, Cooper's fascia; 3, muscle layer and abdominal fascia; 3-1, common tunica vaginalis with cremaster; 4, peritoneum; 4-1, parietal layer of tunica vaginalis propria; h, testicle; s, spermatic duct. Free after Hertwig. B. Section through right half of pelvis with a direct inguinal hernia and a crural hernia, viewed from within; frontal section to the right of midline modified after Rudinger (Topogr. chir. Anat. des Menschen, plate IV, illustr. B). a, Poupart's lig. on cross sect.; this represents the dividing wall between both hernias; b, internal inguinal ring; c, plica epigastrica; d, perpendicular sect. of sac of an internal inguinal hernia. The hollow area between a and 7 is the perpendicular cut sac of a femoral hernia. 1, right common iliac artery; 2, left common iliac vein; 3, Poupart's lig. from within; 4, external iliac artery; 5, umbilical cord; 6, external iliac vein with the inner adjoining lymph vessels and nodes; 7, horizontal ramus of pubic bone; 8, ascending ramus of ischium; 9, muscles on outer side of pelvis; 10, muscles and fascia on inner side of pelvis; 11, lateral section of bladder; 12, prostate; 13, seminal vesicles; 14, lateral section of rectum; 15, vas deferens; 16, external anal sphincter; 17, corp. cavern. of penis (r. side); 18, spermatic cord; 19, scrotum; 20, opened capsules of testicle; 21, testicle and epididymis.

its development. The peritoneal sac is covered by the transverse and the external spermatic fascia.

Acquired inguinal hernias pass downward for various distances. If they remain in the inguinal canal, they are interstitial hernias, if they pass through, they may descend deep into the scrotum (scrotal hernia). For the condition of the testis, see under testis.

In the female, the canal of Nuck is the equivalent of the vaginal process of the peritoneum. Inguinal hernias through the canal alongside the round ligament enter the labia majora (labial hernia).

Of all hernias the inguinal is the most frequent, especially among laborers. These hernias (external) may reach the size of a man's head and reach to the knee and below. Direct hernias are small in comparison to the indirect, and naturally have less tendency to follow the spermatic cord into the scrotum.

In the presence of a hernia in the open inguinal canal, a peritoneal pouching in front of the peritoneum (downward, as a rule) is known as a properitoneal hernia if the downward path of a hernial sac is obstructed, *e.g.*, by a lymph node, and thus lies between the muscles of the abdominal wall; a parainguinal, or an interparietal hernia is the result (see Kausch for nomenclature).

**Crural Hernia (Femoral Hernia).**—The neck of the hernia lies below Poupart's ligament (figs. 337 and 342) between the femoral vein and Gimbernat's ligament. The hernia juts outward below the edge of the falciform process and the cribriform fascia into the fossa ovalis, where the saphenous vein empties into the femoral vein. This permits easy orientation. A femoral hernia is rarely very large. It is usually surrounded by a very firm sac (called by A. Cooper, fascia propria) consisting of fibrous tissue (transverse fascia and fibres of the crural septum) which is encountered by the hernia in its passage. This hernia is more frequent in women. The contents consist of a loop of ileum, merely its wall, omentum often adherent, more rarely the appendix, an ovary, a tube, the gall bladder, a portion of a lobulated liver, etc. (p. 729). A lipoma-like proliferation (fat plug) is often found at the apex of the sac (p. 733).

**Obturator Hernia.**—This is found at the outer and upper circumference of the obturator foramen in the obturator canal. It rarely exceeds the size of a walnut and may be bilateral; it favors women. Only a portion of the bowel wall (usually ileum) is caught in the hernia (Littre's hernia); very rarely a tube or ovary (Schopf, lit.). Pressure on the obturator nerve may be exerted, which lies below the hernia with the obturator muscle and obturator artery; this produces radiating pains (Kaiser). Clinically, obturator hernia is easily overlooked because the protrusion is rarely palpable (Tinner) even at laparotomy, or autopsy.

**Ischiadic and Perineal Hernias.**—These are rare. The latter is due to diastasis of the perineal diaphragm; the former, also called hernias of

the gluteal regions, may be called suprapyriform, infrapyriform, and spinotuberous, according to the position of the apertures (Joessel-Waldeyer), or superior gluteal, inferior gluteal, and ischiatic (minor ischiatic foramen only) (Gorre).

**Umbilical Hernia.**—This is very frequent, and may be congenital because the umbilical cord remains open (umbilical funicular hernia, fig. 343). In marked cases, the intestine, and even the greater part of the abdominal viscera may be forced into the funis (eventration). In eventration, however, umbilical hernia and ventral hernia must be differentiated, the latter due to usually right side defect of the abdominal wall from

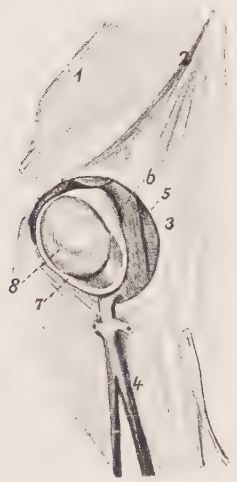



Fig. 342.

Fig. 343.

Fig. 342.—Subinguinal fossa with femoral hernia. 1, external abdom. oblique muscle tendon; 2, Poupart's lig; 3, falciform process fascia lata; 4, long saphenous vein; 5, femoral artery; 6, femoral vein; 7, peritoneum as sac of a femoral hernia; 8, loops of ileum as hernial contents; above the hernia runs the obturator artery 9 (derived from the infer. epigastr. artery) and vein with same name which have been pulled from the abdominal cavity alongside the hernial sack. From Rudinger, Atlas, plate III.

Fig. 343.—Large umbilical hernia (eventration) in a fetus. The hernial walls are formed by the parietal peritoneum and an amniotic layer. It contains liver, stomach, bowels; loops shine through. To left, lateral umbilical vessels; 7/8 nat. size.

defective development of the abdominal muscles (Stephan, lit., Heyn). The umbilicus shows a tendency to hernias, especially in the first year of life. Perhaps funicular pockets remain, but usually they are due to nonresistance of the umbilical scar which develops after the umbilical cord drops off, (usually on the 5th to 6th day). If the hernial ring closes on a part of its contents (usually omentum) the remnant may become a hard nodule or undergo lipoma-like proliferation. Umbilical hernia is rather frequent in multiparous women; the umbilicus is mechanically stretched and the abdominal compression forces the umbilical region outward.

Metastatic tumor nodules are occasionally seen in umbilical hernias. Lit. by Florcken in reference to the appendix as contents.

**Abdominal or Ventral Hernias.** These are most frequent as hernias of the linea alba when the abdominal walls yield to stretching, especially in repeated pregnancies. The stretching of the scar of a laparotomy, or other injury to the abdominal wall is another potent cause. In reference to rare lumbar hernias, congenital (defective growth in the loin, Petit's triangle, *i.e.*, of the lateral abdominal wall) or acquired (traumatic), see Ruppaner (lit.). For more details of this and also of hernia-like ectasias of the abdominal wall, pseudohernias (Borchardt) which are usually caused by partial paralysis of the lateral abdominal muscles (after poliomyelitis, etc.), see v. Baraca (lit.).

### Internal Hernias

In diaphragmatic hernias an abdominal viscus passes into the thorax through an opening in the diaphragm.

Congenital diaphragmatic hernia is due to a malformation of the diaphragm (Broman), often combined with malformation of the liver, lungs, and especially the intestinal mesentery (Hofer). The abdominal contents may push the peritoneum ahead (true diaphragmatic hernia), or they pass freely into the thorax through a hole in the diaphragm (false or spurious diaphragmatic hernia). These latter, actually ectopias or prolapses of abdominal viscera, are far more frequent, and usually situated in the membranous portion of the diaphragm. They develop (according to Liebmann) at the time of separation of the thoracic and abdominal cavities. The true diaphragmatic hernias develop after this separation (lit. by Pape). The defects are often very large. Differentiation between hernia and diaphragmatic eventration, in which the left half of the diaphragm is membranous, stretched, like a dome, is difficult; v. Eggeling-Stintzing and Motzfeldt (lit.) consider especially the relations of the phrenic nerve. The author observed a case (73 year old woman) in which the diaphragm reached to the right 5th rib, and to the left 2nd intercostal space; the stomach and spleen tied together with numerous adhesions were in the cupola of the sac; its color, due to muscular atrophy, was tendinous-white; the diameters of the opening of the sac were 12 by 15 cm. Narrower openings, usually in the fleshy portion, are situated in preformed openings, such as in the foramen of Morgagni, the cleft of Larrey (place to puncture the epicardium) diaphragmatic sternocostal triangle (true sternal diaphragmatic hernia, Eckert, Waelli, Lubosch), at the esophageal foramen (true paraesophageal diaphragmatic hernia; Dubs, lit.), or in the posterior diaphragmatic cleft called Bochdaleki's foramen, between the costal and lumbar muscle attachments. Arranged according to frequency of con-

tents in the thoracic cavity, the relations are: stomach (in the case of Reischauer, a carcinomatous stomach), transverse colon, omentum, ileum, spleen, liver, pancreas, kidney.

Acquired diaphragmatic hernias are always traumatic (fall, victim of a cave-in, stab wound, shot wound, v. Bonin, Oberndorfer, etc.) and usually fatal. The type may be prolapses, or true hernias with peritoneal outpouching, if, *e.g.*, a bullet separated the diaphragmatic pleura and the muscle tendons (Wieting, lit.). In a case published by the author, axial torsion of the stomach after it entered the pleural cavity, caused incarceration (Knaggs, lit. by Iselin; consult also general summary in reference to axial torsion of the stomach by Payer).

Literature by Eppinger, Cailloud, Gruber.

In retroperitoneal hernias (Treitz), the sac is formed by peritoneal folds, into which intestinal loops are forced.

Left and right duodeno-jejunal hernias are usually symptomless and rarely incarcerated (see cases of Vogt and Priebatsch). Behind the duodeno-jejunal fold, they are due essentially to the course of the inferior mesenteric vein (Treitz, comp. lit. by Abbee and Schoppler) which surrounds the left side of the duodeno-jejunal fossa (duod. jejun. recess or sinus venosis, Brosike). This normally comprises only a small part of that flexure, but more and more jejunum may be pushed into the fold which gradually expands and causes the sack to develop to the left; in large hernias the whole ileum may enter. When such a cadaver is opened, a large transparent cyst-like peritoneal sac appears framed by the colon, through which the intestinal loops can be seen. There is no entering loop, only an out passing branch from which the loops can be easily pulled through the large opening disclosing the inferior mesenteric vein along its anterior margin. The author saw a picture, at first glance somewhat similar to this, in a 7 year old boy who sustained a fracture of the femur, and died of ileus of 14 days' duration. The ascending colon, not attached to the abdominal walls, and all of the small bowel, which had a communal mesentery after axis torsion of 360°, surrounded the duodenum and projected loosely through a large absorption cleft in the omentum, poor in fat (atrophic fenestration, Beneke) (publ, by Wandel).

Small hernias must be hunted to the left of the spine (pull out the loops of ileum to the right). A right duodeno-jejunal hernia is rare (Brosike, Schwalbe); the superior mesenteric artery passes along the anterior border of the hernial opening. The sac extends to the right. Merkel (lit.) reported bursting of the sac.

Pericecal hernias occur in the folds in the vicinity of the cecum; these are much rarer and usually without importance, but fatal incarcerations have been reported (Pribram, lit). Waldeyer differentiates superior

ileocecal fossa, inferior cecal (according to Jonnesco, ileo-appendicular fossa) and sub- or retrocecal. The nomenclature of these folds is not uniform (comp. Brosike, Funkenstein). Illustrations by Spalteholz and in the atlas of Enderlen-Gasser.

Sigmoid hernias develop in the inconstant folds in the sigmoid mesentery.

Hernia of the lesser omentum or the foramen of Winslow (epigastric hernia). The foramen of Winslow is the opening between the hepatoduodenal and the duodeno-renal ligaments. The whole of the small bowel, more rarely, part of the colon may enter the opening. No sack is visible on opening the abdomen unless the hernial contents have passed between the layers of the great omentum over the stomach. They are rare and incarceration is also rare (lit. by Jeanbrau et Riche). Occasionally, not the foramen of Winslow (which in the case of Schwolbe was obliterated), but a hole in the base of the transverse mesocolon in front of the spine is the hernial opening. According to Stoltzenberg (lit.), this form of hernia of the omentum goes through a hole produced at a suitably thin place by the pressure of the loops of ileum. See lit. by Federschmidt in reference to these gaps in the transverse mesocolon, those more frequent in the mesentery of the ileum, and their consequences.

Literature of internal hernias in appendix.

### Secondary Changes in Hernias

If the contents of a hernia are replaced permanently as by a truss, the sac may undergo atrophy. An adhesive peritonitis in the sac (from pressure, hemorrhages) is frequent and may obliterate the lumen. This is not rare in younger individuals. The result resembles that of radical operation in which the sac is removed. The shrinking, empty sac is usually pear-shaped and sometimes surrounded by a thick layer of lamellated connective tissue (diffuse fibrosis), but sometimes the fibrosis occurs only where the pressure of the truss is exerted, and is thus annular. In some cases the sac has several rosary-like constrictions, because the narrow neck slips downward and a new neck is developed, which likewise may move downward. The sac may also have secondary niches, and because they are narrow, may incarcerate parts of the intestines, even though the main sac has a wide neck. In the vicinity of these bulgings, the fat-containing connective tissue frequently produces nodular fibrolipomas (hernial lipoma).

Chronic peritoneal changes are frequent in hernial sacs and their contents. White, or thread-like fibrous thickenings may fix the hernia in the sac, and adhesions fuse the intestinal loops into a shapeless clump. The hernia may be reduced "en bloc" (as a whole), *i.e.*, the sac and all are

pushed back into the abdominal cavity, so that, although the hernia persists, the external tumor disappears. More often the contents remain freely movable, pass in and out, and the mesentery, as well as the serosa of the bowel, are covered with a milky white smooth cicatricial coating from the frequent pinching and pulling. Then the mesentery, perhaps also the mesocolon, appears elongated and flabby.

Incarceration is the most important complication of hernias. It will be discussed briefly; for more details consult textbooks in surgery.

FIG. 344.—Huge strangulated inguinal hernia in man 60 years old. Present for 5 days. L. H.

When the contents are pushed forcibly and suddenly (abdominal compression) into the sac so that the ring firmly constricts the contents, an elastic incarceration results (fig. IV, p. 741). When more and more intestinal contents are forced into the afferent limb, until it is distended sufficiently to compress the efferent limb, there is fecal incarceration (fig. III, p. 741).

Incarceration causes the intestinal contents to accumulate in front of the obstruction and to undergo putrefactive decomposition with the

formation of gases, etc., until the afferent loop is enormously distended. This stagnation extends backward to the pylorus, which opens from increasing distension, and the stagnating, fecal, light yellow brown, frothy bowel contents (small bowel) pass into the stomach and are vomited; this fecal vomiting is the most characteristic [late] symptom of occlusion of the bowel (ileus); natural evacuations cease. In reference to absorption, etc., in ileus, see Enderlen and Hotz.

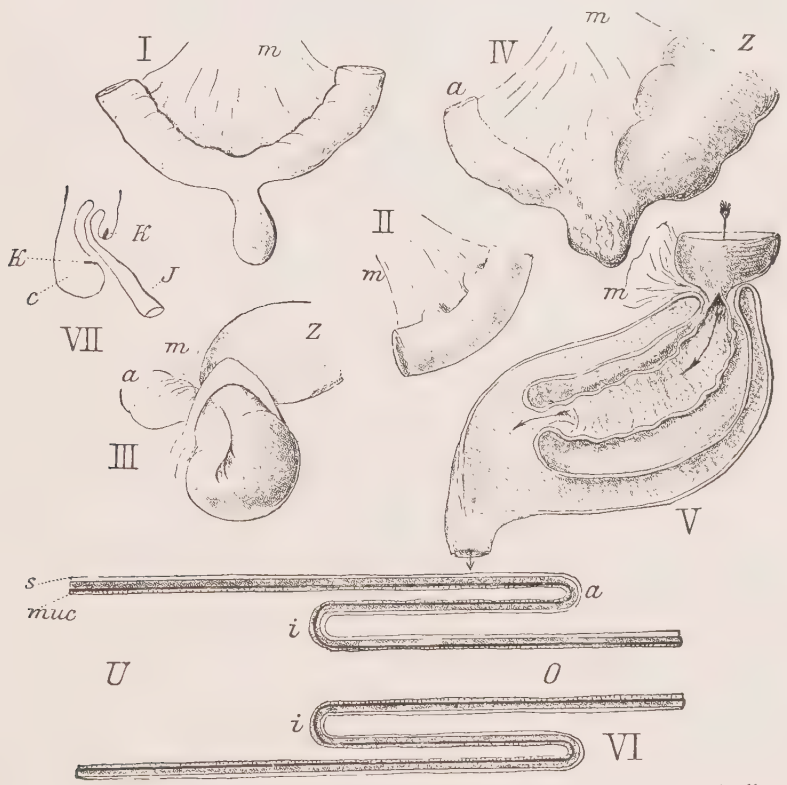
Other consequences are circulatory and nutritional disturbances in the hernial contents and their vicinity. First there is venous stasis from compression of the veins by the neck of the hernia; the incarcerated loops become dark blue and swollen. Since the less easily compressible arteries bring more blood to the parts and the venous outflow is impeded, a serous transudate enters the hernial sac, bowel wall and bowel lumen. Diapedetic hemorrhages also occur from the overloaded vessels, causing hemorrhagic infarction of tissues and discoloring the serous bowel contents. Stasis in the capillaries and veins follows and thrombosis occurs. If these circumstances persist, necrosis and gangrene of the bowel follow, the walls become discolored, brown red, stained by the substances in the bowel contents, especially bile pigment, and the loop becomes soft and fragile. The hernial fluid is discolored, and contains many intestinal organisms. A demarkating suppurative inflammation begins at the border of the dead and living tissue, and fibrinous peritonitis begins in the walls of the sac. If the softened wall ruptures into the hernial sac, a so-called fecal abscess arises which may then rupture externally (fecal fistula). If the incarcerated loop becomes necrotic to any extent, and the afferent and efferent loops are firmly adherent to the hernial sac, rupture of the bowel may occasion phlegmons of the parts covering the abdomen, and fecal discharge externally (unnatural anus). In the depths of the gangrenous sac are two bowel openings, *i.e.*, of the afferent and efferent limbs. An artificial anus is often established surgically above the ileus. If firm adhesions are present at the neck of the hernia, the peritoneal cavity may escape the inflammation.

In other cases a firm constriction of the bowel and mesentery in a narrow opening produces necrosis from constant ischemia. General peritonitis may follow without perforation of the bowel. If only the external constricting ring of the bowel becomes necrotic, the annular decubital ulcer may heal and cause an external cicatricial stenosis of the bowel.

Anemic necrosis is rare, and accomplished by the complete occlusion of both veins and arteries.

**Consequences of Temporary Ischemia.**—Ischemia lasting for some time (hours) leaves the intestinal loop pale and no longer properly vascularized

when the incarceration is relieved. In ischemia of longer duration, the loop dies, since its vessels are permanently impassible; with shorter duration the loop afterwards is hemorrhagically infarcted, because the vessel walls sustain sufficient injury to become permeable to blood. The mucosa alone, as the more sensitive part, becomes necrotic and perhaps replaced by stenosing connective tissue growth (details by Matti), or the whole bowel wall, or only parts, become necrotic with subsequent perforation




FIGS. 345–351.—I. Meckel's diverticulum; m, mesentery. II. Two false diverticuli at mesenteric attachment of bowel, which push between the mesenteric layers. III. Fecal incarceration; z, afferent; a, efferent loops; m, mesentery. IV. Bowel loop firmly incarcerated in the narrow neck of a small hernial sac (elastic incarc.). V. Diagrammatic longitudinal section through an invagination; m, mesentery pulled into the neck; arrows in lumen of bowel. VI. Diagr. of invagination; O, upper; U, lower bowel; a, external turning angle on neck, i.e., turning point on invaginatum; s, serosa; muc, mucosa. VII. Diag. of ileo-cecal invag. (after Leichtenstern). J, ileum; c, cecum; k, ileo-cecal valve, or sphincter.

and peritonitis. After the reduction of an incarceration, and reestablishment of arterial circulation, thrombi may be detached, reach the lung, and establish secondary foci of inflammation.

**Invagination or Intussusception and Prolapsus Recti.**—All the changes under this heading have one thing in common, viz., a part of the intestinal tube is inverted and moved downward. The inverted segment (contain-

ing the bowel wall twice) slips into an adjacent segment which acts as a sheath around the intussusception. Thus three tubes are telescoped into each other. In complete rectal prolapse, the lowest part of the rectum is inverted and pushed outward from the anus forming a sausage-like structure which also contains the bowel wall twice (fig. 352).

FIG. 352.—Iuvagination of ileum into ileum; $\frac{3}{4}$ nat. size. The external bowel (v, vagina) is cut open below; it shows the invaginatum, the inverted bowel with its bowel lumen (the true one); li, corresponding opening; mu, mucosa. The opening has been pulled to the mesenteric side of the bowel sheath; upper lip shorter than lower one; me, mesentery; s, serosa. Above the progressing inner bowel, i enters the vagina (it is somewhat pulled out in this preparation).

In invagination or intussusception, three tubes are telescoped together (see p. 741 figs. V and VI); the outer cylinder is the intussuscipiens or vagina, the two innermost, much folded tubes are the intussusceptum (le boudiu, blood sausage, of the French). In the latter are differentiated the inverted or emerging tube, and the innermost or entering tube. At the neck (figs. V and VI) the emerging tube is inverted and forms the sheath. At the lower free end of the intussusceptum the entering cylinder inverts and becomes the emerging. From the intestinal lumen outward the bowel wall is met three times; the outer and middle tubes touch with their mucosae, the middle and internal with their serosae (figs. V and VI). If two inversions occur there are 5 layers or a double invagination.

The part which enters first always remains at the apex of the intussusceptum during subsequent enlargement. Growth occurs at the expense of the sheath which becomes inverted into the middle cylinder.

The mesentery compressed conically is pulled between the two cylinders of the intussusceptum (see me in fig. 352) and this pull causes the intussusceptum to become concave, with a sausage-like bend at the point of the mesenteric insertion; the bowel opening (mouth, lumen of the inner tube) is pulled to the concave side of this bend (see li in fig. 352).

**Forms of Invagination.**—Invagination as a rule is descending from above downward.

(*a*) Small bowel into small bowel (fig. 352).

(*b*) Small bowel into large bowel (fig. VII, p. 741).

(*c*) Large bowel into large bowel.

The most frequent is ileo-cecal invagination (64% according to Flesch-Thebesius, lit.). Ileum and cecum, with the valve ahead are forced into the colon. The valvula coli, *i.e.*, the ileo-cecal ostium, always moves downward, may enter the rectum and finally prolapse like a plug through the anus. In other cases, (fig. VII, p. 741), the valve remains at its place and the small bowel inverts through it into the colon, *i.e.*, the ileum prolapses through the ostium.

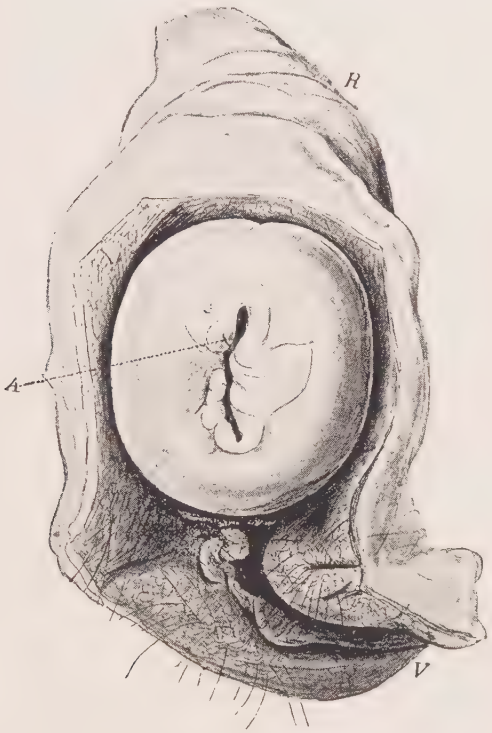



FIG. 353.—Rectal prolapse in a phthisical woman of 30. The ring-shaped, smooth, hard prolapsus was dark red. A, bowel opening; R, rectum; V, vulva with labia; ⅘ nat. size.

Ascending invagination occurs in the appendix (and Meckel's diverticulum), and may produce an ileo-cecal invagination (Pollag, lit.). In reference to its mechanism, see p. 745.

The greatest danger of intussusception consists in the forcing in of the mesentery. Since the vessels of the intussusceptum are compressed by the neck, marked swelling and sanguinous infiltration result from the venous stasis. When the invaginating portion is cut open the intussusceptum appears within like a blood pudding. Necrosis of the mucosa occurs and blood appears in the stools. Further consequences of solid invagination are stenosis, impermeability of the part, dilatation and muscular hyper-

trophy above. Ileus is established. Adhesions or union between the serous surfaces make the intussusception irreducible.

The result varies considerably:

Cure results when the loops are separated. This is probably a frequent cause of the colics of children.

The invagination may be acute (vomiting, bloody diarrhea); death occurs in a few days from incarceration or shock (without peritonitis or perforation).

Peritonitis develops from necrosis of the bowel, especially at the angular places and on the mesenteric side. This probably is the most frequent result.

The invagination may pursue a chronic course in which the intussusceptum is patent.

Under favorable conditions, rarely after one week, usually within 5 weeks of the beginning of ileus, the necrotic invagination may be carried off in fragments, long pieces or as a whole. Union of the separated bowel ends takes place by an adhesive peritonitis at the neck. But later, an annular scar, at the demarkation of the expelled portion, may cause stenosis.

(According to Chiari and Braun, Karpa, Sella, intrauterine intussusception may cause congenital intestinal atresias, or intestinal narrowings.)

If the middle tube becomes necrotic at the upper angle of inversion, or is detached before union is solid at the neck, peritonitis, or peritonitis with perforation, results.

In the dilated bowel above the invagination, necrosis of the wall occurs from stercoral diphtheria; peritonitis is added. This was observed by the author even in simple rectal prolapse. (Septicemia, thrombosis of mesenteric veins, liver abscesses.)

**Development of Invagination and of Prolapse of the Rectum.**—Invagination frequently develops during the agony, especially in children who suffer from intestinal colic, because the peristalsis fades out unevenly (agonal invagination).

Post mortem invagination may occur after sudden death in childhood, because irregular peristaltic movements may continue after death. But the parts invaginated show no congestive reddening; their color corresponds to that of the rest of the bowel, and the invagination can be easily pulled apart.

According to the "paralytic" theory (Leichtenstern), a segment becomes atonic and flabby from catarrhs, peritonitis, previous incarcerations, trauma, etc. The segment above, with active, or even increased peristalsis, moves forward, enters the paralytic segment and invaginates it into the lower active segment. This fits closely around the invaginated

portion and exerts firm pressure on the mesentery (paralytic invagination). If a living segment is simply pushed into a paralytic portion which acts as the sheath, such a compression is impossible. The active segment, forming the sheath by its peristalsis, adds much in propelling the invagination downward (just as it would ordinary bowel contents).

According to the "active theory" (Propping), much in favor today, every invagination is induced by a local spasm of the annular musculature. The segment in contraction elongates somewhat and its aboral end is inserted into the adjoining bowel; this produces the umbrella-like covering. By progressive inversion of the aboral segment, in which peristaltic waves are excited by the primary tetanically contracted segment, the invagination is increased at the expense of the sheath; contractions of its annular musculature cause it to progress oral-wards and thus the amount inverted is increased (Fromme, Flesch-Tebsius, lit.). According to Propping, all invaginations, including those of the appendix, and Meckel's diverticulum, may be explained by this mechanism.

Invagination is sometimes caused by a pull on the mucosa, *e.g.*, by a polypoid tumor (see there and lit. by Kasemeyer and Flesch-Thebesius) (tumor invagination). Nothnagel does not consider that pull is the actual cause, but intensive peristalsis with marked intestinal constriction due to irritation at the place of insertion of the tumor. This may be true of small tumors. Foreign bodies occasionally cause invagination.

Not rarely, the segment above an annular infiltrating tumor (mostly carcinoma) is invaginated into the tumor ring in which there is no peristalsis; this causes sudden obstruction of the bowel.

Spasm of the ileo-cecal ostium (fig. VII, p. 741) is not rare, especially in children with chronic diarrheas, and the active peristaltic impulses of the segment above may cause a common ileo-cecal invagination; or if the sphincter remains firm in its position, the bowel may prolapse through it and (as in ordinary complete rectal prolapse) new portions of the inner cylinder are continuously inverted to the outer. There is a third possibility, viz., an invagination of ileum into ileum, or rectum into rectum, and the part invaginated prolapses though the ileo-cecal or anal openings respectively. In this form of total rectal prolapse, the prolapsed bowel is inverted at some distance from the anus; the palpating finger may be inserted alongside of the prolapsus and past it through the anus into the rectum (exactly as in an ordinary invagination which passes through the anal ring); while this cannot be done in the ordinary rectal prolapse.

Prolapsus recti may also be caused by weakening of the sphincter from chronic catarrhs, and flaccidity of the periproctal connective tissue as in old individuals. The active agent is the abdominal compression as exerted in defecation, or difficult urination, especially in children. The

prolapsus consists of the rectal wall reversed twice and separated by connective tissue. Occasionally this is due to the pull of a tumor (polyp). When the prolapsus becomes old and large, the sphincter atrophies, and the pelvic floor in the retrovesical or retrouterine space deepens into a hernial sac (rectocele).

In anal prolapse only the mucosa and rectal submucosa are inverted. For this reason it has been called prolapsus mucosae recti, in contradistinction to prolapsus recti totius. It is due frequently to hemorrhoids or swollen folds of the mucosa which are forced through the anus during defecation. Naturally there are transitions between rectal mucosa prolapse and complete rectal prolapse. The prolapse may become irreducible by constriction of the sphincter and permanent congestion and swelling of the prolapsed parts. Literature in reference to rectal prolapse by Beresnegowsky.

**Axial Torsion and the Formation of Intestinal Knots (Volvulus or Twists of the Bowel).**—Torsion in the movable segments of the intestines occurs almost always around the mesenteric axis; the limbs of the twisted intestine cross each other; spiral axial torsion in the longitudinal axis of the bowel is extremely rare. The sigmoid flexure is most frequently affected, especially when its mesenteric root, the mesosigmoid, is unusually small because of chronic fibroplastic peritonitis (scars). The ends of a loop are brought close together and form a sort of turnable pedicle (Leichtenstern, von Samson). When the intestine is especially long it is better adapted for such twisting (Lucksch).

According to Heller, congenital abnormal length (megasigmoid) is also a predisposing factor, without close proximity of the ends of the loop (also for Hirschsprung's disease, p. 720; comp. Goebell).

If the colon is not attached normally to the abdominal parieties, or if it united with the ileum by a common ileo-colic mesentery, which is not unusual in the cecum and ascending colon, it becomes very mobile (motile cecum) and including the small bowel shows a tendency to axis torsion and kinking (p. 737). Classification may be made into kinking of the long axis, torsion around the mesenteric axis, and spiral torsion around the long axis of the bowel (Wandel). Literature by Danielsen, Schmidt, Hubner, Eunkie, Klose, Hausmann. Besides torsion, invagination of the common mesentery is also an occurrence.

The site of axial torsion of the sigmoid is quite surprising. The sigmoid flexure, tremendously distended by fluid feces and gas, runs vertically in the abdominal cavity, and may reach the diaphragm and almost completely cover the remainder of the intestines. Its location may be as in fig. 355; if the arrows b and c are reversed they would represent a sigmoid axial torsion.

Torsion of the appendices epiploica may be sufficient to twist them off and release free bodies (see under peritoneum); in incomplete twisting, cords, adhesions, compression of the bowel may result (Riedel, Baruch).

Axial torsion occurs next in frequency in the small bowel, including the entire jejuno-ileum, or individual loops. It is also favored by the approximation of the end points of loops. Mutual pressure of the limbs of the loop on each other may produce impermeability, as does the pressure of other loops on the pedicle.

Torsion of the omentum (Oberst) with, or rarely without previous hernia, also occurs causing congestive hyperemia, hemorrhages into and from the tumor-like thickened, hemorrhagic infarcted omentum or parts of it. Necrosis, final complete twisting off, and other complications have been recorded. (Lit. by Pretzsch, Payr, Riedel, Litthauer, Kohler, lit.)

The formation of knots, volvulus in a narrower sense, may occur between two loops of the ileum, favored possibly by a long mobile mesentery. But it is most frequent between the sigmoid and loops of the ileum, necessitating a long mesentery of the latter, and a short narrow mesentery of the former. The sigmoid twists around the ileum which forms the axis. (Wilms developed interesting opinions about the mechanism.)

### Acquired Changes of the Lumen of the Intestines

**Narrowing (Stenoses) and Occlusions (Atresias).**— These may occur from many causes. Obturation is one, and such occlusions may be caused by foreign bodies (fig. 354), (Borggreve, lit.), fecal masses in the colon (even thickened meconium in congenital ileus, lit. by Fanconi), intestinal parasites (see there), tumors, intussusception, gall stones, (which reach the bowel chiefly through cholecystoduodenal fistulae and become obstructed in the lower ileum which is ⅓ narrower than the duodenum, or in the rectum). Gall stone ileus (lit. by Carl and Lesk, Landow, Krahnstover, Titze, Moller, Wagner) occurs by rare impaction, kinking of a loop, but especially by spasms; as long as the intestine retains its strength, the spastic stenosis proceeds at the same rate as the causative calculus (wandering stenosis, which is sufficient to cause a relative ileus). If the calculus is not expelled in time, exhaustion of the bowel leads to complete paralytic ileus (Propping). Other factors are: strictures due to scars of inflammatory (Goto) and tumor origin, or constrictions and strangulations from without which likewise may be scars of inflammatory origin, pseudoligaments (fig. 355) or tumors which may infiltrate from the outside (p. 823). Inflexions, angular kinkings from peritonitic adhesions, *e.g.*, pericolic (lit. by E. Hagenboch), or post operative, may also be mentioned.

Payr described stenoses of the splenic and hepatic flexures caused by abnormal kinking and adhesions, which produce chronic occlusion clinically resembling intestinal carcinoma (Kuss). Congenital anomalies of insertion of the omentum may be of importance (colic omentum, Haller) in producing adhesions of the omentum to the colon, pericolitic membranes and adhesions to the gall bladder and the appendix (Broman). Nonfusion of omentum and transverse mesocolon is described by v. Haberer. Konjetzny called attention to abnormal mesenteries, especially a duodeno-sigmoid mesenteric plica, causing kinking of the sigmoid. It must be remembered that paralysis of a circumscribed area leads to symptoms of occlusion because the intestinal contents cannot pass the paralyzed area. The causes are manifold which narrow or occlude the lumen by compression from without. If pressure by tumors, and incarceration in internal hernias, are excluded, the chief causes are the various forms of internal incarceration.

Fig. 354.—Obturation of ileum by a pear; bowel wall with beginning gangrene; peritonitis; dilatation above obstruction which was 50 cm. distanct from cecum. The obturated loop was in the small pelvis; man 50 years old; 4/5 nat. size.

Internal incarceration of loops within the body cavity may occur in (*a*) internal hernias, less often in the typical internal hernial sacs mentioned on p. 737, than in the variable recesses of the peritoneum which may be induced by the pull of a shrinking lymph node, etc., in holes or clefts (absorption clefts) in the mesentery (lit. by Prutz, Benn, Federschmidt), mesocolon, omentum or the broad ligaments of the uterus; (*c*) under or around cords stretched within the abdominal cavity caused by clefts or arcade-like pseudoligaments, or peritonitis or appendicitis, or a rolled up omentum, or epiploic appendices, etc. Meckel's diverticulum (p. 726) may be attached to the umbilicus, or anywhere on the abdominal walls, bowel or mesentery and cause incarceration, or the mesocolon may be absent and the omphalomesenteric vessels persist as strands of the mesentery (p. 726). These cords just mentioned form bridges under which loops may slip, or they strap down the base of a loop, or form meshes and clefts into which a loop may slide, or cause annular constrictions or knots, or exert a kinking pull on a loop to which they become adherent.

The segments above a stenosis usually become dilated; the segments below are narrow and empty (no feces pass through) (fig. 354). An intestinal carcinoma may secondarily occlude other places of the small and large bowel (see under intestinal carcinoma; comp. Finsterer). If a segment of the intestinal tract is disconnected by a false anus, it occasionally becomes much narrowed; total obliteration is rare, as described, *e.g.*, by Kaiserling in the sigmoid and rectum.

**Dilatation of the Intestine.**—Circumscribed acquired outpouching of the intestinal walls.

**Diverticuli.**—Diverticuli of the duodenum, usually the size of a cherry to a walnut, rarely larger, sometimes multiple, are found preferably in the descending part, near the papilla of Vater toward the head of the pancreas, and are often due to misplaced pancreatic tissue within the intestinal wall (Linsmayer). Usually they are thin-walled false diverticuli, merely bulgings of the mucosa, without muscularis. Baldwin found true diverticuli. They are very frequent. Sometimes they are developed by traction (Roth). According to Hart, the scars of ulcers may cause pleating of the mucosa and diverticulum-like outpouching chiefly in the vicinity of the pylorus. Rarely, they cause obstructive jaundice (and fat-necrosis, Th. Rosenthal) or subsequent calculus formation (Versmann); consult Clairmont and Schinz.

Diverticuli (false, acquired) of the small intestines are usually multiple, the size of a pea to a walnut, and in contradistinction to Meckel's diverticuli, are attached to the concave side of the bowel lateral to the mesenteric attachment. The muscle layers separate to allow mucosa and submucosa to escape between them. They may force themselves between the layers of the mesentery (fig. II, p. 741) and sometimes show nodular surfaces. The course of the veins decides their location (v. Hansemann); venous congestion, age, increases of pressure, loss of fat, etc., favor their development. The mucosa and submucosa bulge outward into the sheaths of the veins. Rarely, the entire wall is pulled outward by traction of mesenteric scars or tumors in the bowel. An accessory pancreas, lying in its fundus, may pull out a diverticulum.

**Diverticuli of the Colon.**—They are rarely genuine, *i.e.*, only dilatations of the haustra of the colon. They are chiefly false hernial bulgings of mucosa and submucosa through a gap (weak space) in the internal muscular layer, as small, globular or bulbous, thin-walled sacs, situated directly below the serosa, and sometimes still covered by thin longitudinal musculature. The vascular spaces, *i.e.*, where blood vessels, surrounded by connective tissue and fat pass through the intestinal walls, decide their locations. Fecal stasis (chronic constipation), dilatation by intestinal gases (flatulence) and peristaltic pressure cause the dilatation and out-

pouching by pulsion. Telling shares this opinion, while H. Kohn ascribes an influence to abdominal compression. A relation to cardiac lesions in the sense that marked congestion in the venous system might cause increase in the size of the vessel gaps (Graser) and reduce the resisting power of the intestinal walls, was not found by the author, nor by v. Hansemann and Sudsuki. The sigmoid is favored but they do occur further up; the sigmoid may be covered with rows of grape-seed-like granules up to several hundred; their location corresponds to the edges of the longitudinal teniae, but they may also be found within them. These bulgings with narrow or wide necks frequently continue into the lipomatous epiploic appendices and very frequently contain hard round scybala which resemble fecal concretions of the appendix; or they are empty. Consequences: purulent diverticulitis or acute gangrene and perforation may occur but it is rare and is usually of a single diverticulum. When located in the lower sigmoid, the author has seen it lead to suppurative periproctitis (so-called inflammatory tumor, clinically mistaken for carcinoma!) and in other cases to suppurative peritonitis (Arnsperger, lit.). Adhesions, chronic inflammation of the mesocolon perhaps with kinking (Neupert), chronic perisigmoiditis, constricting pseudo-tumors, etc., are other results (Simmonds, lit.). Metastatic liver abscesses have been reported. The author saw a case of the latter kind in a physician 54 years old, abscess the size of a man's head in the right lobe; in a 74 year old man who suffered from constipation for years, rigors developed five weeks before death from liver abscesses (Boehm, lit.). This rather frequent condition was encountered by the author mostly in older people, chiefly males (lit in ref. to so-called sigmoiditis by Stierlin, Honl, Rosenheim, Simons; Franke, Rowlands, de Quervain, Eisenberg, H. Kohn, Simmonds).

Congenital diverticuli of the appendix are rare (lit. Hedinger, Sturm). Other congenital diverticuli (in the new-born) are also considered extremely rare (Heigel, lit.). Acquired false diverticuli (Mertens) are developed with or without inflammation (v. Brunn) not rarely (as shown in fig. 403, p. 839) from the pressure of a hydrops (Konjetzny). Occasionally they force themselves between the layers of the meso-appendix (Mundt).

**Diffuse Enlargement of the Intestinal Lumen.**—Marked enlargement of the colon without stenosis is unusual but is described by Verse in senile atrophy; it strongly resembles congenital megacolon (p. 720). Partial dilatation without stenosis is sometimes seen in a very mobile colon (colon mobile) due to insufficient fixation and it presents varying forms (Hausmann).

Dilatation of the bowel over larger areas is seen most frequently above narrow or occluded areas. If the narrowing is gradual, muscular hypertrophy is developed behind the stenosis and probably compensates to a

degree, especially since peristalsis is increased above the stenosed area; later, insufficiency is the rule; the musculature becomes atonic, or grossly degenerated.

If motility is stopped, the contents accumulate above the obstruction and dilatation results. The contents at once undergo abnormal decomposition by the numerous intestinal bacteria, most active of which are probably anerobes (Pommer); gases are formed (meteorism) and these contribute to the dilatation. It is also favored by reduction of muscle tonus, and the atonic wall yields readily to the increasing internal pressure. Chyme collects in the small bowel (comminuted food material mixed with gastric secretion) in large quantities and stagnates and decomposes. The contents become thin, poultaceous and foamy. Decomposition processes are much more intensive in the small intestine. Normally no protein decomposition occurs in the quickly moving contents of the small bowel; in its upper part the reaction is acid, but it gradually becomes alkaline in the jejunum. Intestinal bacteria are relatively few in number, but absorption of food is rapid. On the other hand, putrefactive organisms are undisturbed in the sluggish, alkaline contents of the colon. It has been mentioned under incarceration of hernia (p. 739) that overfilling of the bowel is soon followed by escape of gas and fluid into the stomach, eructations and fecal vomiting. From these stagnant putrid contents, the products of protein decomposition such as aromatic bodies, are absorbed and appear in the urine, among them indican and phenol. Indican is easily detected and found abundantly in stenoses of the small bowel. Auto-intoxication is also increased by the absorption of bacterial toxins from the contents (lit. by Clairmont and Ranzi, and consult for causes of death in ileus Braun-Boruttau; against the intoxication theory and criticism, see Enderlen and Hotz, lit.).

Other causes of dilatation are acute paralyses of the musculature which may develop, *e.g.*, in acute peritonitis. Stagnation and meteorism appear promptly. In some cases, the musculature is but relatively insufficient as in acute constipation; if the quantity of contents is extremely large, the bowel may be unable, however active, to propel its contents forward (relative insufficiency); finally it becomes paralytic and absolutely insufficient. In a case at Breslau, absolute insufficiency of the colon followed by ileus developed in a strong young man after acute excessive partaking of poppy seed dumplings which filled the colon to the thickness of an arm, (cf. Peukert, who saw severe lesions of the mucosa and perforation). Markedly fermenting bowel contents are especially likely to cause paralytic ileus (Walther). More often, however, insufficiency of the intestinal musculature is due to chronic overloading with food, and chronic constipation (general review by Rost) which may be accompanied by coprostasis

especially in the colon; sometimes the musculature is poorly developed in the very beginning or the atrophy is a sequel to chronic catarrhs. If the paresis is primary and the coprostasis and symptoms of ileus are the result, it is called paralytic ileus.

As a rule, the dilated and thickened segments above the stenosis of older cases develop a stercoral diphtheria which leads to ulceration and perforation (sometimes multiple), usually through a minute opening; this is followed by suppurative peritonitis. Kocher gives those ulcers which appear in dilated parts the special name "dilatation ulcers;" they

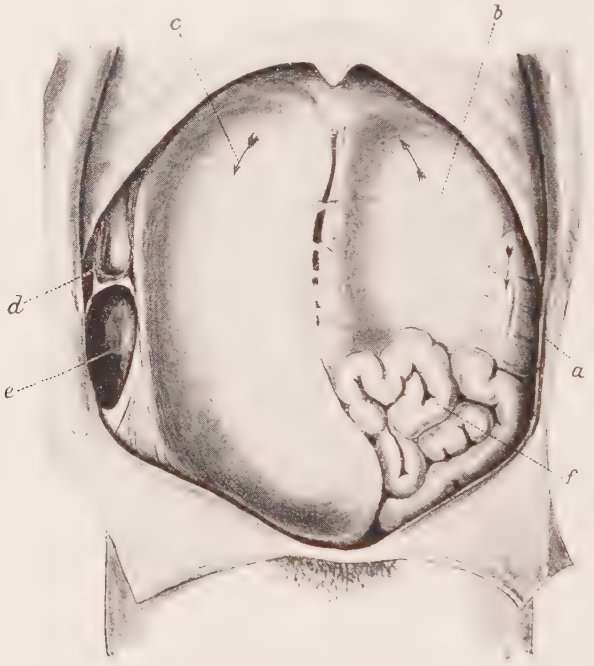



FIG. 355.—Enormous dilatation of the raised sigmoid flexure constricted at its end points by adhesions. Its limbs are connected bridge-like by numerous adhesions. a, descending colon; b, upper; c, lower limb of sigmoid flexure; the latter reaches behind the symphysis; the rectum joins it directly. Adhesions between bladder, base of sigmoid and posterior pelvic lining. d, gall bladder; below this an encapsulated fecal abscess, (e), covered anteriorly by the abdominal wall; below this the ascending colon; f, loops of small bowel lying anterior to the ascending limb.

are especially frequent in the cecum and are sharply cut; according to Prutz the stretching of the vessels interferes with venous backflow, causes congestive hyperemia, thrombosis, hemorrhages, necrosis and ulcers; in addition bacteria are supposed to penetrate more readily into the distended wall, thus adding changes in the vessel walls followed by thrombosis (Ebner, lit. by v. Greyerz, Meidner, Hofmann, Shimodaira). This conception must indeed be accepted for the fluid in an overstretched bowel, but in other cases it is explained by the toxic necrosis from the chemical

effect of the stagnating feces plus secondary bacterial development (stercoral diphtheria) or by a follicular or catarrhal (phlegmonous) ulceration (comp. under dysentery and fig. 384) (see also Sauer). The cases of enormous dilatation behind stenoses of the bowel, pictured in figs. 355 and 391, show that the whole dilated segments are most extensively ulcerated; the mucosa remained only in fragments and the muscularis was exposed almost everywhere. In both cases a peritonitis developed due to perforation. In a carcinomatous stenosis of the sigmoid flexure in a 65 year old man, the author saw an enormous dilatation of the colon which contained thick clay-like poultaceous material; this mucosa was smooth but the markedly dilated ileum was thickly sprinkled throughout its whole length by follicular ulcers. Perforation was found in an ulcer situated about 20 cm. from the valve; peritonitis. But in cases with hard scybala and collapsed bowels, pressure necrosis is the only correct explanation (see Gobiet). The author has seen cases in which the obstructing, stony hard scybala produced ulcers which actually were imprints of the fecal masses. In segments which have become anemic by pressure, the bacteria multiply and ulcerative disintegration results with eventual perforation. In a case of fecal impaction (48 year old man, constipated for 8 years) the author found a hard coprolith 39 cm. in diameter, as large as a fist, dry within, situated above the rectum, simulating clinically a true tumor. The sigmoid contained numerous pressure ulcers around the coprolith; it is proper to speak in these cases of actual stercoral trauma. Such ulcers may also be found among other places in the ampulla of the rectum (see there). A distension ulcer may also develop in a bowel segment made inactive by operation, and may perforate, if its contents have insufficient drainage. The author saw a case in which the cecum and ascending colon had been short circuited on account of fistulae; a perforation had developed in the colon the size of a pinhead. The mucosa was smooth and pale. Not rarely the first result of perforation is a sacculated fecal peritonitis, a so-called fecal abscess (fig. 355-e) from which the acute general peritonitis eventually develops. But a fecal abscess may perforate externally or into the bowel.

### Circulatory Disturbances

**Active Congestive Hyperemia.**—At autopsy, individual loops, especially those in the pelvis, may be found richer in blood, due to hypostasis.

The mucosa which generally is anemic, gray white or gray yellow is spotted bright red, most marked around the follicles or in folds and villi. Frequently the serosa and part of the underlying muscularis is the chief site of the active hyperemia; many injected, delicate vessels are visible, stretching in the longitudinal axis of the bowel, or branching in circular

courses. Active hyperemia is the beginning of all acute intestinal inflammations, but very little of this can be seen in the cadaver. The bowel is diffusely red in cholera.

**Passive Hyperemia. Stasis.**— The mucosa is swollen and blue red, especially on the tops of the rugae; in chronic congestion it is dirty brown red and slaty; the submucous veins especially are markedly filled. Small hemorrhages into the mucosa or into the bowel lumen are common, causing bloody or chocolate colored discoloration of the contents. These small hemorrhages extending in striae on top of the rugae leave the pigmentation mentioned above. The intestinal veins participate in congestion of the portal circulation (especially so in diseases of the liver) as well as in general circulatory disturbances due to cardiac and pulmonary diseases.

Compression of intestinal veins in incarcerated hernias, invagination, etc. was mentioned on page 740, and the consequences of such compression consist of hemorrhagic infarction of the bowel walls, stasis and thrombosis, exudation of fibrin and partial (only the mucosa) or complete gangrene of the bowel wall. For post operative thrombosis, see p. 664. Extensive hemorrhagic infarction of the small bowel (description see p. 755) may follow thrombosis of the portal vein (descending mesenteric thrombosis, truncular thrombosis; Weil). For example, in a 42 year old woman with calculi in the common duct the author saw thrombophlebitis of the portal vein. The discolored gray red thrombus had descended and caused hemorrhagic infarction of the small bowel with the exception of 50 cm. of the upper jejunum. There were fresh red thrombi in the superior mesenteric vein and its ramifications. Primary thrombosis of the superior mesenteric vein also occurs, (Amos, lit., Lindner, Mauclaire et Jacoulet, Bolognesi, lit.); a septic thrombus develops in the mesenteric veins (thrombophlebitis) due to infection from the bowel lumen and extends into the venous branches. The symptoms are pain, ileus, intestinal hemorrhages (the author found the latter absent at times), all corresponding to occlusion of the artery, but peritonitis may dominate the picture.

In very marked chronic congestion, but occasionally also independent of it, (according to Moller, lit., as a rule in old people), many small varices of the submucous and subserous intestinal veins are scattered throughout the entire small bowel representing little saccules filled with fluid blood or thrombi. Bennecke believes they are congenital phlebectasias, Okhubo hemangiomas. Large varices are rare. The author, for example, saw in a 54 year old man a smooth globular varix as large as a cherry invading the lumen of the upper ileum.

In reference to hemorrhoids, see under veins (p. 165), and under rectum (p. 841).

**Edema of the Intestinal Wall.**—This is not only a result of stasis, but also of congestive hyperemia. It is always present in chronic inflammation of the mucosa, and appears frequently in acute inflammation of the mucosa and serosa as well. As a rule the fluid saturates the mucosa and submucosa which appear jelly-like and translucent. The rugae of the jejunum and colon are thick, quivering, transparent rolls. In the ileum also the swollen mucosa may rise in rugae.

Acute edema of the walls, especially of the ileum, is not rare in acute peritonitis and not only the walls are infiltrated but the fluid in the contents is considerably increased, the bowel filled to capacity; when it becomes paralyzed as it does quickly in peritonitis, it likewise becomes markedly dilated. It is characteristic of inflammatory edema that the layers are easily separated from each other; the bowel can easily be pulled out of its serosa at autopsy and the walls are easily torn.

In chronic stasis (cirrhosis of the liver, heart lesions) the edema at times is enormous and the walls of the heavy and dilated upper loops of the small bowel may approach 2 cm. in thickness; they appear gelatinous on cross section. But the bowel may also have hard and thickened walls and be somewhat contracted.

**Embolic and Thrombotic Processes in Intestinal Arteries.**—Occlusion of the trunk of the superior mesenteric artery by embolism or the much rarer autochthonous thrombosis results in grave disturbance of the blood supply and nutrition with hemorrhagic infarction of the distended (p. 751) small bowel. Its wall is dark red, sanguinous, saturated with edema and therefore tense and thickened; its mucosa is blood stained diffusely or in spots; the contents are liquid, foamy, bloody or chocolate brown. Necrosis and gangrene make the wall thick, swollen, red, infiltrated by hemorrhages, later brown and finally soft, friable and easily torn. The mucosa, covered with a bran-like coating, becomes ragged and is detached. Ileus may develop during the course of the disease and it is quickly fatal from hemorrhages or peritonitis. The portion of the bowel undergoing the hemorrhagic infarction and necrosis depends upon the position of the arterial occlusion.

Non-infectious embolism of the superior mesenteric artery (Polya, lit.) occurs in endocarditis, thrombi in the left heart and atheroma of the aorta, also subsequent to thrombosis of the aorta no matter how slight the damage in this vessel (fatty degeneration of the intima) or in the mesenteric artery itself; thus thrombosis of the mesenteric artery may be autochthonous in arteriosclerosis of this artery or may be conducted from the aorta.

The general appearance of cases of occlusion of the arterial trunk resembles that of thrombosis of the superior mesenteric vein (p. 755; Gobiet). For details of the anatomical and microscopic findings in intes-

tinal infarction, see Pommer. For clinical data in reference to these diagnostically difficult problems, see Bolognesi, Trotter; for experiments, see literature by Bolognesi. Comprehensive presentation, literature and good diagrams by Reich; also Ceelen.

Thus hemorrhagic infarction follows arterial occlusion, even though the superior mesenteric artery is no end artery in Cohnheim's sense since there are anastomoses with the inferior mesenteric and the pancreaticoduodenal arteries. Therefore Cohnheim and Litten (assuming a venous reflex) called the vessel a "functional end artery;" the collaterals are relatively small at the start and cannot carry sufficient blood before the walls of the vessels deprived of circulation have become permeable; thus the blood, supplied collaterally, passes out of the vessels and causes infarction in the tissues. In embolic occlusion of the inferior mesenteric artery (its branches are the left colic and the superior hemorrhoidal arteries) circulatory disturbances are unusual because the collateral supply arrives promptly. Simultaneous occlusion of both the superior and inferior arteries is very rare (Merkel, lit.).

The superior mesenteric artery supplies the jejuno-ileum and the ascending and transverse colon, *i.e.*, the parts derived from the umbilical loop, the mid gut of the embryo. The descending colon, sigmoid and rectum, developed from the hind gut, are supplied by the inferior mesenteric and the common pudendal arteries.

Anemic infarction is very rare from embolism (lit. by Matthes); it requires total obstruction of the arterial blood supply including the collaterals to the tiniest (wall) branches below the anastomotic arches (see experiments of Marek). The author saw it occur in 20 cm. of the upper jejunum while the rest of the small intestine was hemorrhagically infarcted and sharply demarkated from the anemic, necrotic, white-gray-yellow segment. All the arterial branches, even the smallest, in the walls of this piece were plugged; the mucosa was emphysematous, green, and brown. In many vessels of the hemorrhagic part there were long obstructing plugs; this was found in a 64 year old woman with thrombosis in the upper aorta; death from peritonitis. The vein also is eventually thrombosed, but this is secondary and non-essential as Niederstein describes (Boinet).

The consequences of operative and experimental mesenteric detachment as a rule are similar to those of arterial obstruction. See Haberer (lit.) in reference to details and important anatomical variations in the ramifications of the mesenteric arteries in man and dogs.

Non-infectious embolic occlusion of small arterial branches causes isolated small (curable) or larger circular hemorrhagic infarcts.

Small infarcts are due to occlusion of the smallest twigs of the mesenteric artery on the far side of the arcades of communicating anastomoses;

larger infarcts (breadth of a thumb and more) always involve a number of branches on the near side of the vascular arches, or within them, and obstruction must be quick and simultaneous; otherwise the collateral circulation takes care of the nutrition. In annular infarcts, ileus may develop (lit. by Deckart; Tatke).

At the given place, the bowel wall quickly becomes dark red and thickened; as soon as necrosis appears the mucosa hardens and becomes gray and cloudy. The necrotic mucosa is then detached, leaving a transverse, usually circular, ulcer which may heal to a slate gray pigmented scar, finally with annular stenosis, or the wall becomes necrotic throughout its entirety, permeable to intestinal bacteria and possibly perforated, which results in peritonitis.

Schloffer produced circular ulcers and scars by ligation and severance of vessels in rabbits. Ulcers appearing both in the intestines and stomach following all sorts of abdominal operations are considered due, among other things, to direct or retrograde thrombosis in the arterial and venous channels; see under stomach, p. 664; Bolognesi. Infectious embolic occlusion of smallest arterial twigs (*e.g.*, endocarditis) causes small hemorrhages, diphtheritic or ulcerative foci (Michaelis) or abscesses (so-called embolic enteritis). The latter are often found in large numbers in the mucosa of the small bowel and of the colon, to the size of a lentil or smaller, frequently surrounded by a hemorrhagic zone. The author saw them in pyemia (staphylococcus), after thrombophlebitis of the angular facial vein (furuncle), localized transversely to the long axis of the bowel opposite the mesenteric attachment. At times the emboli may consist only of bacteria. Internal rupture of the abscesses results in small ulcers; abscesses in the wall may lead to peritonitis. In a 26 year old woman with ulcerative aortic endocarditis, the author saw macroscopic emboli in the arterial twigs near the mesenteric attachment of the upper jejunum; forked from the occluded artery were circular discolorations, blue brown, speckled with yellow spots; the mucosa had green scabs on the transverse rugae. See Oberndorfer, Hart in reference to acute embolic enteritis.

In rare cases, miliary and somewhat larger aneurysms of the minute intestinal arteries are encountered, clearly visible when the bowel is held against the light; they are easily mistaken for varices. According to Ponfick, multiple aneurysms may be of embolic origin (p. 147).

In other rare cases a nodular periarteritis (p. 121) may cause ecchymoses, erosions, infarction and necrosis from which develop multiple ulcers of the mucosa and deeper layers eventually leading to peritonitis and quick death (Zimmermann, Lorenz, Verse).

**Hemorrhages.**—Hemorrhages occur in the intestines from active or passive hyperemia, hemorrhagic infarction (see previous chapter), embol-

ism in malignant endocarditis, in various inflammatory processes and ulcerations (dysentery, typhoid fever, tuberculosis, follicular and catarrhal ulcers, tumors); punctate hemorrhages of the mucosa and even larger submucous hematomas occur in the hemorrhagic diatheses such as leukemia, hemophilia (Foderl saw intestinal stenosis from submucous hematomas), scurvy (von Hansemann, Sato and Namba), septic diseases, intermittent fever, burns and various poisonings (arsenic, phosphorus, sulphuric acid, mercury, etc.). Amyloid of the vessel walls leads to hemorrhages, usually small, especially in the colon; they leave a dirty gray pigmentation. These diapedetic hemorrhages in rare cases may increase to clinically observable intestinal hemorrhages.

Fatal diapedetic intestinal hemorrhages, analogous to those of the stomach (p. 664), are observed at times in pronounced interference with the portal circulation, especially in cirrhosis of the liver; as in the stomach, the source of the hemorrhage which comes from many small vessels, perhaps cannot be found. Finally foreign bodies and trauma may cause intestinal hemorrhages. See p. 165 for hemorrhoidal bleeding; hemorrhages of melena neonatorum on p. 663.

Blood in the bowel (p. 664) is quickly expelled in red foamy stools, or is thickened in the colon to a tarry black mass (melenia) in which no red corpuscles can be recognized.

In a case of bleeding in the esophagus (p. 634), the colon contained a single blood clot as thick as a thumb, 112 cm. long, modelled by the haustra and teniae, pitchy, ropy, black red in which erythrocytes could still be recognized microscopically.

Hematoidin may remain in the superficial layers of the mucosa directly below the epithelium producing brown and later slate colored pigmentation (containing iron-hemosiderin). See page 804 in reference to iron-free brown pigment.

Bismuth stools may be black; stools containing iron are not black from iron sulphid because sulphuretted hydrogen is exceptional in the human intestines, and then present in quantities too small to give the reaction of iron sulphid; these stools darken on contact with air due to oxidation (Quincke).

### Inflammation of the Intestines. Enteritis

Inflammations of the separate parts are called duodenitis, ileitis, typhilitis, appendicitis, colitis, sigmoiditis, proctitis.

**Catarrh of the Bowel (Catarrhal Enteritis).**—In acute catarrh the mucosa is spotted red, edematous, swollen, loose, cloudy and covered with sero-mucous, muco-purulent or purulent exudate mixed with desquamated epithelium showing cloudy, granular, hyalin or mucoid changes.

Some of the desquamation is post mortem. If the desquamation is marked as especially in the colon from which connected membranes are detached, it is called a desquamative catarrh, as frequently seen in children with summer diarrhea. But desquamation also occurs in catarrhs of the small bowel, *e.g.*, in arsenic poisoning, cholera, dysentery, and may be so marked that the stools contain thimble-like coverings of the villi. Serous saturation and cellular infiltration of the mucosa are combined with increased secretion of the mucosa. The lymphatics are also involved. There is enlargement of the follicles and agminates, but in children who have frequent intestinal catarrhs, it must be remembered that the normal follicular apparatus is always more plainly in evidence than in adults.

In the severe, acute, infectious catarrhs of the bowel (p. 760), all the layers may be involved; small cell infiltrations (and bacteria) follow the lymph channels and the peritoneum itself may become diseased. The author saw a number of astonishing cases of this kind, especially in children who died of diffuse purulent peritonitis after a very severe diarrhea of short duration (permeation peritonitis). Erkes saw the same in adults with acute diseases of the mucosa. The mesenteric lymph nodes are usually acutely hyperplastic. Lennander and Nystrom found pneumococci in such cases which the author also found in some. Invasion may also occur from the appendix. Animal experiments have demonstrated the permeability of the intestinal tract to bacteria in spite of former doubts; (Rzegocinski, Wrzosek, Ficker, comp. Tavel). We must distinguish between (*a*) passage through the walls of the bowel to the peritoneum, (*b*) passage through the walls into the lymph nodes, (*c*) passage into the blood (Hornemann, lit.).

Chronic catarrh may supersede the acute, or appear insidiously. Most chronic catarrhs are due to the congestion of cardiac and liver diseases.

The most important changes are similar in many respects to those of chronic gastritis. The brown, slate gray, to black pigmentation is striking, especially in the apices of the villi (melanosis of villi) and in the vicinity of follicles which are surrounded by a dark halo. Peyer's patches contain gray black spots.

While most of the pigment is considered due to local hemorrhages, Hueck assumes there is absorption of iron derived from blood or bile. The black discoloration is due to sulphuretted hydrogen (pseudomelanosis, p. 659). Villous melanosis, however, may be present without inflammation.

In so-called pseudomelanosis due to inflammation or hemorrhage, or according to M. B. Schmidt, to a hemolytic pigment formation, the solitary and agminate follicles are brown to black. The pigment contains iron.

The interstitial tissue becomes cellular and proliferates (hypertrophic chronic enteritis), and may later contract. Frequently the interstitial

inflammation is chiefly in the mucosa between the glands, but the submucosa and muscularis also may show marked invasion by young connective tissue.

In rare cases, the connective tissue hypertrophy is so diffuse and so pronounced that the lumen of the bowel is narrowed (probably first at the valve of Bauhin).

Polypoid elevations of the proliferating mucosa analogous to those in the stomach appear chiefly in the colon,—polypoid enteritis. Some polyps contain glands which undergo cystic dilatation by retention of secretion. Polypoid proliferation is not rare on islands of mucosa in the vicinity of old ulcers. It is most frequent in dysentery (fig. 361, p. 775), but also occurs in tuberculosis.

Many chronic catarrhs cause atrophy and thinning of the mucosa and not rarely the muscularis (chronic atrophic enteritis), beginning first in the glands which in consequence of repeated desquamation partially or completely lose their power of regeneration and thus become shorter or disappear entirely; at the same time the interstitial tissue, previously hypertrophic, shrinks and leaves the mucosa thin, flat, hard and slate gray in color. The villi of the small bowel undergo atrophy; the muscularis simply atrophies or undergoes fatty degeneration.

According to Nothnagel, 80% of adults have a more or less extensive atrophy of glands, especially in the cecum, but Gerlach has shown that the pictures of Nothnagel are artefacts (p. 805).

The lymphatics of the walls frequently show chronic inflammatory changes (p. 174); see Creazzo in reference to Auerbach's plexus in subacute and chronic catarrhs.

But acute and chronic catarrhs may independently localize to isolated portions, especially the duodenum, cecum, appendix and rectum; see paragraph, diseases of intestinal parts (p. 828 ff.).

The causes of catarrhal inflammations are manifold; we may first consider changes in the contents, and second, hematogenous injuries.

The contents themselves may cause inflammations, *e.g.*, from chemical decomposition products, such as organic acids from carbohydrates; stagnant contents undergo abnormal decomposition and develop irritating substances but they also allow increase in the usual intestinal organisms which in turn cause irritation, both by their metabolic products and by increasing the decomposition. The contents at times irritate merely mechanically, *e.g.*, if the food without containing causes of inflammation, is especially suitable for fermentation, or if it is an especially favorable culture medium for the intestinal flora. At other times, both pathogenic and non-pathogenic bacteria (see p. 858, under intestinal parasites) enter with the food and cause abnormal decomposition of the intestinal contents, or produce

irritants or toxins or even penetrate the mucosa (for instance staphylococcus enteritis) and produce intestinal sepsis (Bollinger). In other cases toxic inorganic and organic substances are introduced with the food, *e.g.*, corrosive poisons in weak concentrations such as arsenic.

Among organic poisons, those of meat, fish, cheese, muscles (mytilism) may prove fatal in a few hours (Schmittmann). Meat poisoning may be differentiated into (*a*) meat (often chopped meat) spoiled from the start, coming from infected or otherwise diseased animals killed just before they would have died, containing bacillus enteritidis (Gartner) or the closely related (details by Weber and Haendel) bacillus paratyphosus B., (Schottmuller), which is the most important, according to the opinion of many (comp. Babes); (*b*) meat, at first good, later spoiled (1) by ordinary saprophytes (proteus vulgaris, colon bacillus) or (2) by pathogenic organisms, especially the extremely resistant, ubiquitous (Huebner-Rimpau), paratyphoid bacillus B. (Schottmuller) which may also infect other food such as milk, cereals, preserved beans. The food may appear wholesome, *i.e.*, may not give the impression of being spoiled (lit. by Loele). These cases usually run a subacute course and gastrointestinal symptoms such as vomiting and diarrhea are prominent.

B. paratyphosus B. (Schottmuller, Huebschmann) is differentiated into (1) an enteric cholera-nostras type (paratyphoid gastro-enteritis), and (2) a clinically typhoid form (abdominal paratyphoid); (1) it was formerly taught (Loele, lit.) that the typhoid form is rarer and usually runs a benign course like a mild abdominal typhoid fever with some differences from typhoid fever such as affecting chiefly the colon, neither selecting nor so intensively attacking the localized intestinal lymphoid apparatus, nor so consistently and intensively involving the mesenteric lymph nodes and spleen, but new experiences, especially in the war in which the typhoid type predominated, have taught that paratyphoid may perfectly imitate abdominal typhoid both macroscopically and microscopically, even to bacillus-containing rose spots (Eug. Fraenkel), but it does attack the colon more frequently than abdominal typhoid (Sternberg, Jaffe, Pick, and especially Wiesner, lit.). This similarity extends to the changes in the liver (miliary foci) and kidneys as well as to the form and localization of the complications, among which suppurative processes have an important share; in fact, Pick believes they are worse than in abdominal typhoid, and involve kidneys, bones, gall bladder, urinary bladder, renal pelvis, muscles, parotid gland, prostate, etc. (Martens). (2) In the paratyphoid gastro-enteritis the acute or chronic catarrh is much more pronounced than that which accompanies abdominal typhoid; shallow ulcers favoring the colon appear in the inflammatory hyperplastic lymphoid apparatus, or independent of it; they differ from true typhoid ulcers both in location and

shape. The mesenteric lymph nodes and spleen are markedly swollen (Pick) or slightly so, or not at all (Herxheimer). Occasionally, a dysenteric form is developed, but it is perhaps due to a combination of dysentery and paratyphoid (Beitzke). The differences in the typhoid and enteric types (there is also a mixed form) are probably due to blood stream invasion in the typhoid form (Marchand) and enteric localization in the enteric form (v. Wiesner). According to v. Wunschheim, the paratyphoid bacillus is also the cause of distemper in dogs.

The paratyphoid bacillus A was formerly regarded in Germany as of little importance, but it has gained greater recognition since the war. It has been clinically and bacteriologically investigated exhaustively by Erdheim and Schopper (lit.). Shorter incubation time (2–7 days), rigor, which appears early in more than 50% of cases, early diarrhea, distension of the abdomen often appearing as early as the second day with pain and meteorism, eruption of rose spots on the second day, the course of the fever, repeated relapses, absence of delirium and stupor, less kinds and severity of complications (bronchitis, lobular pneumonia) all differentiate paratyphoid A from true abdominal typhoid. The prognosis is favorable. Anatomically, there are acute enteritis without follicular involvement and acute splenic tumor.

In the acute catarrh of the bowel (p. 758) and in the chronic catarrh (p. 758) bacteria multiply in the body of the patient (true infection), while in the acute condition the trouble is due essentially to ptomaines (Brieger), which are developed in decomposing proteins under the influence of putrefactive organisms (B. proteins,etc.); these are poisonous substances of the alkaloid series, unchanged even by boiling. Ptomaines cause chiefly gastrointestinal symptoms or nervous symptoms, such as paralyses of selected smaller and delicate muscles of the eyes, pharynx, tongue, larynx, etc., and may cause death with the symptoms of bulbar paralysis. Distinguished by the severity of the nervous symptoms, perhaps after a passing attack of vomiting, is the classical botulism, or so-called sausage poisoning, because the first observations were made on cases of sausage poisoning. The effect is due to the action of the botulinus toxin, while the bacillus botulinus producing it (van Ermengems, lit)., an anerobic saprophyte which infects and multiplies in the food, does not increase in the body of the patient. See Burger in reference to the demonstration of the poison in the stomach of the cadaver. The B. botulinus infects all sorts of meat (raw ham), fish, and other foods, especially preserved vegetables (olives), but the food shows no noteworthy changes. The course is acute, death is frequent, mortality about 60% (Dorendorf), chiefly from paralysis of the respiratory center. Microscopic changes are seen only in cases of some duration in the form of nuclear disintegration and destruc-

tion of cells of the central nervous system (Burger). When the meat (or other food), besides the bacteria, contains large quantities of specific toxins (which do not change by boiling), with acute and chronic catarrh the symptoms of exceedingly acute meat poisoning may develop. The finding of paratyphoid bacilli in food, however, does not positively identify them as pathogenic, since there are forms which are harmless to man but cannot be differentiated from the pathogens (Hubner). According to Komma (lit.), their presence at least proves unsanitary methods in handling meat, since most of these organisms probably come from the intestinal tract of the slaughtered animal. Conradi states that food substances may be infected by human carriers (lit. in appendix).

The color of the thin diarrheal stools of intestinal catarrh is quite variable; they may be pale, white or stained with non-reduced bile pigments, or contain mucoid masses discolored yellow or green or bloody. The diarrhea due to calomel which checks reduction and decomposition is characterized by green stools, that of cholera, by white, gruel-like discharges.

Diarrhea may occur without catarrh due solely to accelerated peristalsis, induced, *e.g.*, by nervous influences, since the quantity of normal digestive juice is quite considerable. Laxatives may cause an increase in intestinal motility and diffusion (diffusion catarrh).

It must be remembered in reference to diarrheal stools, that the catarrhal intestinal mucosa is less able to absorb fluids especially when peristalsis is very active; furthermore the intestinal wall secretes abnormally, *i.e.*, pours out an inflammatory exudate and intestinal juice. The latter is especially true in cholera.

**Special Changes in Acute and Chronic Intestinal Catarrh.**—Follicular enteritis. The intestinal lymphatic apparatus is more or less involved in every inflammation of the mucosa; in some acute catarrhs the follicles and Peyer's patches are much swollen and hyperplastic (simple, hyperplastic, follicular enteritis), as occasionally in children with pharyngeal diphtheria, and in cholera. The follicles may become as big as peas, and the Peyer's patches as prominent as grapes if the nodules chiefly are swollen and the intermediate tissue escapes. If everything is uniformly hyperplastic, they become as though harrowed. In less severe cases, the follicles, edematous and infiltrated with cells, are glassy and look like pearls; if the round cells are more abundant, they become thicker, pale, gray and cloudy. If only the internodular substance is increased and the nodules themselves are unaffected, the so-called "surface reticuleé" develops, with its net-like appearance. The same reticular appearance is seen when the follicles of an hyperplastic Peyer's patch undergo regres-

sion before the interstitial tissue. Small hemorrhages are common in and around hyperplastic follicles and leave behind a gray, brown or black pigmentation in the form of punctates and coronas (p. 759). While the nodular enteritis just mentioned depends on hyperplasia and may heal perfectly, a severer form, the apostematous follicular enteritis, usually chronic in character, and selecting the colon, is characterized by small shallow ulcers produced by suppuration and rupture of the follicles as further changes. These are follicular abscesses and ulcers, so frequent in fecal stasis (fig. 383, p. 814) and dysentery, although according to Lohlein and Torinus, the ulcers in dysentery are derived not so much from the follicles as from intranodular gland proliferations (see below) which undergo secondary suppuration. There is no doubt that this process is often active, but Orth, Westenhoffer and others cling to the idea of follicular ulceration (see Lohlein). The small rounded ulcers, the size of hemp seeds to lentils (lenticular) and corresponding to the shape of the follicles, are yellow, and surounded by a red inflammatory areola, anatomically difficult to differentiate from typhoid in small children. They are often present in large numbers. The edges are sharp, without much swelling, but they are soon undermined because the mucosa is detached over considerable areas by purulent infiltration (phlegmon). This form of ulceration is called sinuous, and the extensive undermining of the edges is well seen if water is poured on the surface. On the other hand, such sinuous ulcers may be caused by the internal rupture of parietal abscesses and this must be recognized. Finally, the mucosa is perforated like a sieve. Confluence of submucous abscesses or nodular abscesses or both, produces large concave (sinuous) areas of destruction, with submucosa or the villous muscularis as the base. They have some resemblance to tuberculosis. Many ulcers are framed by thin bridges of mucosa in more extensive cases. The bases of older ulcers, older chiefly in the colon in follicular dysentery, are often pigmented gray. Since the mucosa and the deeper layers up to the serosa are infiltrated and the bowel wall thickened, perforation seldom occurs. Small ulcerations may heal to smooth slaty scars, but the larger ulcers may show little tendency to heal; final cicatrization occasionally causes stenosis. The remnants of the mucosa may undergo hypertrophy and become polypoid (fig. 361).

Small cysts in the submucosa are especially frequent in dysentery (p. 773); the cavities of follicular suppuration are covered with an epithelial layer derived from neighboring glands, and the epithelium may proliferate into glands in the base of the cavity. In these small cysts (deep cystic colitis in contradistinction to superficial cysts, see Orth) the production of mucus is active (goblet cells); Koster believes the mucus in the follicular pits is a product of the mucosa secreting into the empty

spaces (Heubner); Beitzke thinks the cysts are due to secondary covering of dysenteric ulcers, but in many cases another explanation is required. Both physiologically, and especially after inflammation, as in dysentery, there are intranodular gland proliferations in the colon (see above), *i.e.*, ingrowths of epithelium into the submucosa within a follicle, (fig. 356); these may become dilated to a cyst containing mucus. When the cysts are numerous and close together, the mucosa bulges in bosses from

Fig. 356.—Cystic dilatation of glands which penetrated into a lymph node; small cell infiltration of mucosa and submucosa; necrosis and fibrin coating on surface of mucosa. From rectum with dysentery; man 40 years old; (medium magn.).

which project small clumps of mucus like grains of sago or frog eggs; they may be expelled and appear in the stools. The iodine reaction differentiates them from starch granules, since starch turns blue on contact with iodine. Potato fragments coated with mucus may look similar (Ullmann).

The mucosa is sometimes thickly infiltrated with pus cells, the tissue suppurates (ulcerates), and disintegrates superficially. These are the so-called catarrhal erosions and ulcers of changeable form and grouping; further progress may mean phlegmon of the submucosa and extensive

liquefaction of the inflammatory tissue as seen so frequently in the appendix (p. 834). The severest forms occur in dysentery. Small, fresh, catarrhal ulcers (lenticular) are shallow, rounded losses of substance with their margins but slightly infiltrated; larger ulcers have slaty pigmented bases with calloused margins. A superficial erosion of the mucosa may be followed by follicular or circumfollicular suppuration or by diphtheritic inflammation. Thus the so-called catarrhal ulcers appear in acute and chronic inflammations of the intestines.

Obstruction or narrowing of gland outlets in an atrophic mucosa causes stagnation of secretion and subsequent cystic dilatation (chronic cystic enteritis, fig. 357). The cysts are usually small, like dewdrops, glassy

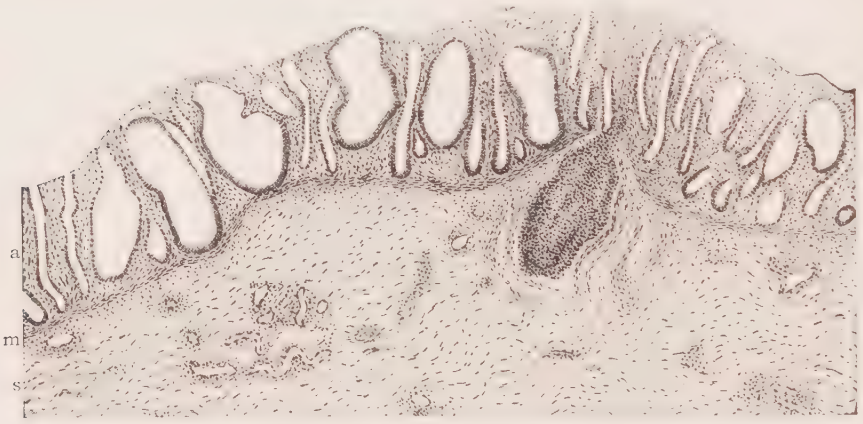



FIG. 357.—Superficial cystic colitis; a, mucosa, small cell infiltration. Surface epithelium is macerated (post mortem change). Some Lieberkuhn's glands dilated, one bulges on the surface m, muscularis mucosae. A lymph follicle projects from the submucosa (s) into mucosa (a). (Low power.)

and multiple; their size is that of a pinhead or lentil, rarely larger. On pressure or puncture the viscid mucous contents escape (cf. cystic gastritis, p. 667); rarely the dilated cysts filled with mucus are so close together that a circumscribed portion of the mucosa is changed into a quivering gelatinous mass easily mistaken for mucoid carcinoma.

In mucous colitis (Nothnagel), the feces show "attacks" of mucus discharged as membranous tags or tubules or noodles, compressed in the folds of the colon.

A small number of cases may be traced to the chronic cystic enteritis mentioned above, but in most cases the epithelium of the glands of Lieberkuhn (goblet cells) produces the mucus, stimulated by a pathological irritation (Kaabak and Rosenschein, lit.); the mucus expelled from the gland lumena reaches the surface to fuse with that of adjacent glands into a membranous layer. v. Noorden accepts the opinion of many who

view it as a secretory neurosis, *i.e.*, a secretion anomaly of the colonic mucosa often observed in hysteria and neurasthenia (analogous to bronchial asthma); it is also spoken of as "mucous enteritis," or "muco-membranous enteritis" and less fittingly as "membranous enteritis." Signs of inflammation are absent; the occasional mild infiltrations of the mucosa (Rothmann) must be considered secondary, accumulations of eosinophiles to the contrary notwithstanding. These structures are occasionally sent in alcohol for examination and the membranous tags or casts become wrinkled, opaque and white; they must first be softened in water which swells the mucin, and then unfolded. The identification is often of practical importance; at first glance they may be taken for worms ("pseudohelminthae"), or mistaken for fibrin. But the addition of acetic acid makes mucin cloudy, fibrinous, striated, granular; in fact it coagulates, while fibrin becomes glassy and clear. Weigert's so-called fibrin stain colors both (A. Schmidt, lit. by deQuervain).

### Appendix

Cystic intestinal pneumatosis (first described and named by Mayer in the hog) also called "air bubble mesentery" or "intestinal emphysema," is a rare chronic affection in which gas-filled vesicles, and partly pedunculated bladders up to the size of beans are found, often in great numbers, mostly below the serosa, especially in the ileum, but in Neugebauer's case only in the colon. They are frequently adherent to adjacent loops by fibrous threads and membranes. The submucosa and certain preferred parts of the peritoneum also may be cushiony, spongy and thickened (Tuffier and Letulle). The gas is produced in the lymph vessels of the submucosa and serosa, and is squeezed from the latter in the form of bullae; the mucosa is secondarily pushed outward. Histologically, the early stages of these gas cysts show proliferation of lymph vessel endothelium and active formation of giant cells (foreign body irritation of the gas), (cf. cystic colpohyperplasia under vagina). Opinions are divided in reference to the origin; (*a*) the theory of infection considers it probable that the pneumatosis is due to gas-forming non-pathogenic microbes; this is opposed by cases in which careful cultural examinations proved negative. (*b*) The mechanical theory assumes that injuries of various sorts create entrances through which intestinal gases are forced into the bowel wall by intraabdominal pressure. Recently Faltin, Schnyder, Steindl (lit.) have supported (*a*), while (*b*) is accepted by Miyake, Demmer, Kuder and Hey. This affection has no relation to septic gas phlegmon (see under puerperal fever), nor with decomposition. The course is benign (absorption of gas). (Lit. by Orlandi, Dupraz, Grondahl, Finney, Nowicki, Dietrich, Arzt, Urban, Martini, Ciechanowski.)

**Pseudomembranous (Fibrinous or Croupous and Necrotizing, So-called Diphtheritic) Intestinal Inflammations.**— A solidifying fibrinous exudate is deposited on the surface of the mucosa as (1) the croupous form; or the disease is not confined to the formation of a fibrinous pseudomembrane, but immediately develops a more or less deep necrosis and scab formation in the mucosa as the (2) so-called diphtheritic form.

It has many causes (p. 770), but very rarely indeed the diphtheria bacillus, as in true pharyngeal diphtheria (p. 608).

True croupous enteritis (1) is rare, but is occasionally found in infections, especially of puerperal origin; the fibrinous pseudomembranes may be fairly thick and firm and, as a rule, are stained yellow green or brown by the feces.

FIGS. 358–359.—A. Cross section through colon in dysentery, free after Rindfleisch. Normal longitudinal folds of mucosa (pl) and the thickened sanguino-serous infiltrated submucosa (s) form rigid projections directed into the bowel lumen; ps, sigmoid plicae; t, taeniae; r, ring musculature, contracted. B. Diphtheritic inflammation of bowel; a, mucosa; b, submucosa; c-1 and c-2, muscularis; d, serosa; e, cross section of glands; f, scab; g, softened exudate. (Low power.)

In diphtheritic inflammations (2) there are (*a*) superficial bran-like coatings or sandy deposits, easily wiped off the hyperemic mucosa; the pseudomembranes consist of fibrin, superficial necrotic mucosa, epithelium, leucocytes and mucus, and (*b*) deeper necroses of the mucosa forming a thick compact scab with the superimposed fibrinous masses of exudate; they are somewhat raised, penetrate more or less into the depths, discolored green or brown by feces, or red by blood pigment, while the bowel wall as a whole is thickened and stiff.

Gluge originated the striking comparison (Vogt): the mucosa resembles the cracked, moss-covered bark of a tree.

The scab and the parts it covers contain large numbers of various bacteria. The base under the scab shows small cell infiltration, the submucosa is wide, hyperemic, edematous, and frequently shows hemorrhages and fibrin. The scab itself is unstainable and remains as a faintly refractile mass in which the tissue outlines are visible here and there or not at all. The smaller arteries are hyalinized.

Such diphtheritic inflammations are localized especially in the colon along the longitudinal folds corresponding to the teniae (fig. 358) or to the crescent-shaped transverse folds; these are the parts which come in contact during contraction and are therefore in closest touch with the contents. The arrangement produces figures resembling a rope ladder or

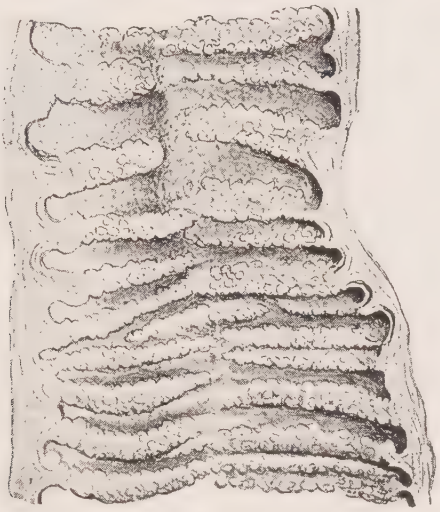


Fig. 360.—Fresh diphtheritic inflammation of ileum; nat. size.

steps. If the parts in between are also involved, the mucosa resembles the stomach after ingestion of a corrosive, or a relief map of mountain ranges. The flexures are usually selected for the severest effects, also the rectum and other places where fecal stagnation is common. Involvement of the small bowel produces thick folds (which, however, are not the folds of Kirkringi), from inflammatory swelling of the mucosa and submucosa to which the scabs are attached like garlands (fig. 360). Their detachment leaves ulcers; if deep, they heal by cicatrization and may cause strictures.

The undestroyed mucosa between the gray, serpentine, ulcer scars sometimes undergoes hyperplasia to small polyps (chronic polypoid enteritis; pp. 764 and 774).

Follicular diphtheria localized to the lymph follicles is much rarer; among other complications it may appear in true dysentery. The scabs are on the apices of the follicles, penetrate uniformly into the depths,

become detached as a whole leaving small, uniformly round, sharp, and rimmed, shallow ulcers as though artificially gouged out (like typhoid ulcers).

The conditions under which diphtheritic enteritis appears are as follows:

(1) true dysentery in which it may be called primary (p. 771, etc.);

(2) various infectious diseases or previously existing diseases of the bowel, thus in pyemia, especially puerperal fever (the superficial fibrinous form), in cholera (in the small bowel), in typhoid fever, tuberculosis, more rarely in small pox, and very rarely in true laryngeal diphtheria.

(3) Fecal stasis (stercoral diphtheria) liberates active factors, such as, bacteria in putrefactive decomposition, chemical products of decompositions, occasional mechanical pressures, but only insofar as they cause minute abrasions and circulatory disturbances in the mucosa making it less resistant to inflammatory factors; very hard scybala, however, sometimes cause deep pressure necroses and large ulcers. The changes in simple coprostasis are seen most frequently at the flexures of the colon, in the appendix, sometimes in the female rectum, above stenoses, as, for example, carcinomatous, above an artificial anus, above a prolapsed rectum, and even above the normal anus. The mucosa is inflamed and necrosis or gangrene supervenes; the ulcers may perforate and lead to peritonitis. For distension ulcers, see p. 752.

4. Chemical substances such as are formed in uremia, ptomaine poisoning (p. 762), arsenic (severe symptoms in a 23 year old man who had been intensively treated with arsenic for lymphogranulomatosis), bismuth, mercury, may cause diphtheritic inflammation of the bowel; the clinical intestinal symptoms may be identical with those of primary dysentery. If the expressions, diphtheria (diphtheritic inflammation), and dysentery, are used promiscuously, as is often the case, as for instance "mercuric dysentery," true dysentery must then be spoken of as "primary," *i.e.*, true dysentery.

In uremia (see under nephritis), the diphtheritic inflammation, especially of the ileum, but also exclusively of the colon at times, is considered due to ammonium carbonate which is a decomposition product of urea excreted into the bowel (Fischer, lit.; Grawitz, Thierauch). (This excretion of urea which also takes place through the stomach and the skin in uremia, is called "compensatory.")

In mercury poisoning (any compound introduced), the severest conceivable degrees develop in the colon; but it is neither constant, nor always confined to this part. The lower portion of the ileum may also be involved, or, exceptionally, it alone is affected (as the author described). The entire internal surface of the wide, thick-walled colon is covered in

continuity with a quite uniform, thick, dark green, puffy scab. The only comparably intense change is that due to direct corrosion with acids in the stomach. The author attempted to show that it is not due to the corrosive action of mercury excreted by the bowel, although both the mucosa and the rest of the wall are pigmented (details by Almkvist), but because mercury poisoning produces stasis and results in the formation of hyalin thrombi in capillaries with sufficient circulatory disturbances to render the intestinal mucosa non-resistant to the invading intestinal bacteria. The quantity of ingested mercury necessary to cause very severe intestinal diphtheria and death, are often much too minute to cause such erosive effects as they are excreted, and besides, excretion is only partial through the bowel; in addition, cases occur in which very large doses were taken and death occurred after some days without pathology in the colon. This interpretation has been disputed by others (Falkenberg); Heinz supports it, compare Kionka, Elbe, Almkvist, Burgi, Priebatsch. Ricker is of the opinion that mercury irritates the vaso-motor system of the intestines and also the kidney (Weiler, Strache, lit.) and causes vascular dilatation, slowing of the current, stasis and subsequent necrosis. Direct corrosion of the bowel by mercury is very rare (comp. the author's observation, p. 675).

5. In operative procedures such as resections, making an artificial anus, direct infection from without may cause intestinal diphtheria.

*Phlegmonous enteritis* as an independent disease is rare, and usually occurs in the duodenum and upper jejunum, rarely the colon, which, in v. Saar's case, was a thick, stiff, edematous tube. Death is usually due to peritonitis. All the layers are infiltrated with pus cells and fibrin, the submucosa especially so. The mucosa is edematous and gray yellow. The process may extend to the mesentery, pancreas and the hilum of the liver. Staphylococci and streptococci are the organisms most frequently found. The etiology is enterogenous, *i.e.*, secondary to existing simple or tuberculous ulceration, or primary, with the portal of entry not demonstrable, or hematogenous (rare) (lit. by Frising and Sjovall, Glans, W. Muller, Hellsfrom, Ingier). Compare with gastric phlegmons. Literature and observations by the author in reference to jejunal and gastric phlegmons.

### Specific Infectious Diseases of the Intestines

**Dysentery.**—In the temperate zones, the disease is sporadic with occasional epidemics; in the tropics, it is endemic. While the ameba dysenterica is the cause of tropical dysentery, the epidemic dysentery of northern climates is due to the bacillus of dysentery. Amebic and bacillary dysentery may be combined.

The term dysentery is frequently used as a clinical conception (Quincke) to cover dysentery-like symptoms of many etiologies (lit.

by Just), but the designation dysentery (true) should be reserved for the etiologically and pathologically anatomically well defined disease (Adelheim, lit. Sternberg). If we speak of dysentery broadly, we mean amebic or bacillary dysentery.

Opinions are divided as to the process of infection; per os has been unequivocably demonstrated in laboratory experiments with amebae (Lohlein), and this is usually considered the chief route (Grober, Burgers and others); Beneke, however, thinks a more important portal of entry is the anus. Lohlein considers this question still pending.

**Amebic Dysentery.**—Endemic dysentery, carefully studied first in Egypt, is an hemorrhagic catarrh of the colon, not rarely involving also the lower ileum, with the formation of ulcers, typically rounded, with swollen or acutely gangrenous walls, often very large, with undermined edges; diffuse gangrene is occasionally developed (Kuenen, lit.). The alterations are severest in the cecum and not in the rectum as in bacillary dysentery; they diminish in intensity downward. As initial changes, Lohlein described infarct-like necroses of the mucosa, the size of pinheads to peas, dull yellow and bulging. This is followed by disintegration of the tissue, commencing at the boundary of the mucosa and submucosa, while in bacillary dysentery the destruction is suppurative-necrotic, but the changes become similar as soon as secondary bacterial infection is added to the amebic effects. In these situations, Losch, Koch, Kartulis, and others, found the amebae constantly (fig. 423) together with bacteria, especially streptococci and forms of colon bacilli, to which were assigned an active participation in the destruction, but, according to recent ideas, bacteria have no special influence on the character of the process, and the pathogenic amebae are solely responsible (Hara). This is the entameba dysenterica—histolytica—or tetragena (20 to 60 mcs. in size), the mature cyst of which is characterized by 4 nuclei (for staining see Riegel, Wiener; in reference to forms of entameba, see Hartmann) quite different from the harmless intestinal amebae (entameba coli) the encysted form of which is characterized by 8 nuclei. The pathogenic ameba has been found in North America, Italy, Russia, Japan, China and other countries. Amebic dysentery is sporadic everywhere, often transmitted by "carriers" which the world war helped to distribute (lit. by W. Fischer). The amebae coli are found in abscesses of the liver, usually in the pus, with or without bacteria (Kartulis and others). In older experiments, the colons of cats were injected with bacteria-free pus from hepatic abscesses and with human feces; Hara produced typical dysentery in cats by feeding them the feces of patients. Thus far, however, this ameba has not been grown in pure culture. The animals can be found in the mucus of the stools, often in large numbers (Kruse and Pasquale), in the intestinal mucosa (Christof-

fersen, Hammerschmidt), in the ulcers (Kruse and Pasquale), in the deeper layers of the intestinal wall, even where no severe inflammatory symptoms have as yet been produced; they invade the lymph- and blood-vessels of the intestinal wall (veins of the submucosa, Lohlein) from which they may be carried to the liver (metastatic invasion, see Justi, lit.). In feces and in the intestines of the cadaver, the amebae perish in a few hours (lit. and illust. by Bose, also by Dopter, Ruge and Esau, Kuenen, Lentz, and lit. in appendix).

**Bacillary Dysentery.**—In the intestinal contents of cases of epidemic dysentery, Kruse found a bacillus easily cultivated on ordinary media, differing from the typhoid bacillus which it otherwise resembles by being thick and non-motile (Jaeger). Flexner and Shiga found identical organisms in tropical dysentery, but various subtypes have been identified such as the Shiga-Kruse, the Flexner, the Y type and others (Lunz, Ghon and Roman; lit. by Dopter, Lentz, Ludke, Sikl and others). Kruse differentiates another non-toxic pseudodysentery bacillus, the cause of "pseudodysentery," a sporadic disease, occurring as dysentery, among others, in the insane in asylums, due to lack of desire to evacuate; it differs from the true dysentery by lack of blood in the feces and by the mildness of the attack (other opinion by Shiga, see Haenisch, and opposed Heuser). To demonstrate the organism in the feces requires fresh material (Friedemann). According to Sikl (lit.), the bacillus may be cultured from the mucosa in most cases, while forms poor in toxins may be secured from the liver, spleen, lymph nodes. The ulcers invite important mixed infections (Gross).

**Various Forms or Stages of Intestinal Changes in Epidemic Dysentery.**—The changes of dysentery are confined chiefly to the colon, but in ⅓ of the cases, the lower ileum is also involved, very rarely the latter alone (Jaffe). They vary greatly in intensity and extent, are most pronounced in the aboral parts of the colon, especially the rectum, and different stages occur side by side. For the characteristics of amebic dysentery which frequently involves the appendix, see above.

Throughout some cases (catarrhal dysentery) and at the beginning of all, there is an intensive catarrh of the colon. The mucosa and submucosa are thickened by a sanguino-serous infiltration; the hyperemia, the edematous saturation and the cellular infiltration of the submucosa are much more aggravated than in simple catarrh and may involve the other layers. The mucosa is covered with glassy mucus and desquamated epithelium, easily wiped off, is reddened in spots, swollen, loose, soft, easily pulled off. The mucus may show an admixture of blood.

Death may result from severe intoxication; the process may recover or it passes into the severer forms running protracted courses.

In severer cases, the epithelium is necrotic, mixed with leucocytes and covers the mucosa with a branny layer (superficial necrotic pseudomembranous inflammation). Entire tubules lose their epithelial cells in flakes looking like maggots (Rokitansky) contained in a thick purulent sanguinous exudate. The sero-sanguinous infiltration becomes seropurulent, leads to necrosis, liquefaction and disintegration of the mucosa, which is cast off in larger or smaller fragments. The ulcers are shallow and superficial, or deep and sinuous with undermined margins which reach to the muscularis. Their size varies between the diameter of a pea and that of a silver dollar. Smaller ulcers are less common. Their shape and localization are quite haphazard. While most of the ulcers are merely from liquefaction without typical localization, there do occur typical follicular sinuous ulcers and submucous mucous cysts (p. 764) which come from follicular abscesses, or from abscesses following intranodular gland proliferations (p. 764). Sometimes they dominate the anatomical picture (follicular dysentery), most frequently in advanced stages of the disease. When extensive submucous phlegmons are added to the ulceration, probably from secondary infection, (cocci, etc., Lohlein, Sikl), there is widespread undermining, rounded, sieve-like, or cleft-like, ruptures upward through the mucosa, placed transversely to the intestinal axis; as neighboring ulcers coalesce, the mucosa is reduced to bars, bridges, railings and networks.

In the severest cases, there is so-called diphtheritic inflammation of the intestine, a necrotizing, or deep pseudomembranous enteritis, or even an extensive gangrene (gangrenous dysenteric enteritis). The ulcers remaining after scabs and gangrenous parts are detached have red to black bases due to small hemorrhages, and may assume enormous proportions. The relatively healthy, but red and puffy portions of mucosa remaining, are arranged almost diagramatically like the steps of a rope ladder, but are reduced in size from both sides until they stand out quite prominently from the surfaces of the ulcers. When the ulcers heal to smooth scars, usually beginning in the upper colon, the retained islands of mucosa become very prominent, polypoid, as in fig. 361, or actually adenomatous from gland proliferation (intestinal polyposis). Justi described a rare, markedly hyperplastic polyposis. Sometimes, much connective tissue is produced in the bases of the ulcers in which the peritoneum takes part, thereby preventing perforation. Occasionally, unprotected ulcers perforate or slowly developing ulcers covered by pericolic adhesions lead to peritonitis or peri- or retrocolic abscesses (lit. by Chiari). Beneke mentions multiple distension tears from meteorism.

The healing of mild stages of dysentery (catarrh, softening, follicular abscesses) results in slate gray, flat scars. The deeper gray scars of diph-

theritic ulcers are often zig-zag in shape, the result of more connective tissue formation. But stenoses due to scars are rare (lit. by Chiari), more likely to occur in the rectum, but in an observation of the author, throughout from the splenic flexure to anus (I. Diss, Schulte). The bars and bridges of mucosa may persist as thickened polypoid landmarks with the peculiar appearance of being a fringy, meshy, net-like neoplasm. Chronic dysentery offers pictures which can be recognized as specific recurrences, usually of less intensity and extent. Sikl believes bacillus-containing mucous cysts and submucous abscesses are responsible for the continuation of the specific process.

FIG. 361.—Intestinal fat polyps after extensive dysenteric ulceration. Bowel hypertrophic and dilated. Between the remains of mucosa, which has undergone polypoid changes, is the muscularis covered with scar tissue. Man 23 years old; ¾ nat. size.

The classic symptoms of dysentery, as far as the intestine registers, are colicky pains, muco-sanguinous stools and tenesmus; the general symptoms (Brauer) are considered due to absorbed specific toxins. As to the course, there are quickly fatal cases; some convalesce in about 6 weeks, and others persist for months or years. Schimdt and Kaufmann differentiate clinically an ulcerative, a pericolic spastic, and a dyspeptic form of chronic dysentery. The anatomist encounters the severe ulcerative cases most frequently. Long continued suppurative ulceration produces amyloidosis. For the surgical treatment of ulcerative colitis, see Chiari, lit.

The intestinal discharges are not uniform; some are gray or yellow white, sero-mucous, mixed with small fragments; others are creamy and odorless; there may be 20 to 60 or more stools a day (Grober); this type has been called "white dysentery," if blood is admixed, "red dysentery." The hemorrhages may be profuse and dangerous. See Lohlein in reference to the characteristic sago-like mucous clumps (p. 765). Both white and

FIG. 362.—From a patient 28 years old, a soldier who had travelled extensively, especially in the tropics. The history states he had dysentery but is not clear as to the type, but probably was amebic. He was brought to the hospital in extremis from intestinal obstruction and at autopsy the entire colon was found densely packed with feces, obstruction beginning at the ileo-cecal valve. On opening the large bowel, the condition as shown was discovered. It represents a healed dysentery with regeneration of the mucosa, but regeneration carried to such an extreme that bridges and tabs, strings, cords, and papilloma-like excrescences are formed. These were present to varying degrees throughout the large bowel. Histologically, they consisted of connective tissue covered by a single layer of columnar epithelium with little or no attempt at gland formation. The mucosa between and under these growths was flattened and atrophic. Such conditions must not be mistaken for neoplasms such as papillomas or fibro-epitheliomas. A and B are drawn from the corresponding places in the lower diagram which is a portion of the transverse colon; $\frac{1}{4}$ nat. size. C is a cross section drawn in elevation of the position marked; $\frac{3}{4}$ nat. size. Many hard and softer masses of feces were entangled in the net-like growths and it was with difficulty that many of them were removed.

bloody stools may occur at the same time in the same individual. If the process is complicated by putrefaction, the stools become brown green and extremely fetid. In reference to liver asbcesses, especially in amebic dysentery, see under liver.

**Cholera.**—In Asiatic or Indian cholera, as an epidemic disease, the most important anatomical change is an acute inflammation of the mucosa, principally of the small bowel, but occasionally in the colon and even in the stomach, varying in degree from a simple catarrh to diphtheritic changes. The intestinal changes themselves are so little characteristic that the correct diagnosis of cholera must be made by the finding of cholera bacilli, microscopically and culturally. They are found in the bowel contents and the mucosa. The infection is per os.

The cause of Asiatic cholera is the comma bacillus, spirillum or vibrio, discovered by R. Koch in 1883, which is found in the dejecta of every early case of cholera. The dejecta are the most important sources of infection. Virulent comma bacilli in the water or food reach the intestinal tract of susceptible individuals, and, after an incubation period of 1 to 2 days, cause cholera, or perhaps only a slight intestinal catarrh. No symptoms appear in immune individuals, although specific bacilli can be demonstrated in the stools (healthy carriers, Adami and co-workers). Convalescents may be carriers for weeks to several months and carriers themselves may contract the disease (Sternberg). A cholera epidemic follows the arrival of the first infected individual by progressing from focus to focus or explosively from a contaminated water supply. Koch has demonstrated the bacillus in swamp pools in India where cholera is endemic.

The vibrios of cholera are ½ to ⅔ as long as tubercle bacilli, but thicker and possess a terminal flagellum; besides the comma form, S shaped bacilli are often seen. They stain readily with fuchsin, etc., and are Gram negative. Spirillae forms are not seen in preparations made directly from bowel contents, but appear in bouillon or peptone water cultures. After some hours a delicate film grows on the surface which is often a practically pure culture. The spirillae also form long spirals in media. This technique is recommended, especially when the number of cholera bacilli is small, as in stools. The bacilli grow in an alkaline medium with abundant water, best at a temperature of 25° to 37° C. They are killed in ten minutes at 60° C. They withstand lower temperatures very well, but if multiplication is desired in the cultures, the temperature should be at least 18° C. Drying kills the bacilli quickly, *e.g.*, in 2 hours on the human hand; the same is accomplished by quite weak disinfectants (2% carbolic acid in a few minutes). Quite weakly acid culture media prevents growth, likewise the normal gastric juice containing about 0.2% hydrochloric acid. But in moist surroundings, such as damp

wash, dejecta, river water, etc., the bacilli may remain alive for weeks and months (Gildemeister and Baerflein).

On gelatine plates (best at 22° C.) typical colonies appear in 20 hours as scalloped bordered, rounded spots, light yellow with slight irregular surfaces and a peculiar lustre suggestive of small heaps of very minute glass fragments (Koch). In gelatine stab cultures a globular liquefaction funnel is produced which slowly sinks downward. Other spirillae resembling those of cholera, *e.g.*, those which Finkler-Prior occasionally found in cholera nostra, and those which Deneke cultured from cheese, quickly liquefy gelatine; the other biological characteristics of these bacteria do not correspond with those of the comma bacillus; the same is true of Metschnikoff's gamaleia vibrio and others. But, nevertheless, especially in peptone water (enriching procedure) certain cholera-like bacilli appear which morphologically and biologically resemble true cholera vibrios. For this reason, other methods must be employed to identify the true vibrios. These are: (*a*) Pfeiffer's method of bacteriolysis. Briefly this is as follows: blood serum of guinea pigs or goats, which have been immunized as thoroughly as possible against cholera endotoxins by several months of treatment with cholera bacilli, is much diluted with nutrient bouillon. This mixture is the reagent. A loopful of a 20 hour agar culture of the vibrios to be tested, is mixed with 1 cc. of this reagent, and the mixture injected into the peritoneal cavity of a young guinea pig. At 5 minute intervals drops of the contents of the peritoneal cavity are removed by capillary glass pipettes and examined. If true cholera bacilli are present they are seen in the hanging drop, or on the stained slide as small globules which finally dissolve without traces in the fluid of the abdominal cavity (in 20 minutes). According to Pfeiffer, this dissolving process is the specific action of cholera antibodies. The control consists of only the doubtful culture, thinned with bouillon and normal serum; if cholera bacilli are present in the abdominal cavity, they are living and motile. Differentiation is also done of the colonies grown on agar by means of a high potential agglutinating serum which permits agglutination of true cholera bacilli in very weak dilutions of 1 to 2000 to 1 to 5000. (More details by Koch, Kirchner, Kolle (Min. Blatt, f. d. preuss, medic. Angeleg N. 12, 1902) and by Kolle and Gotschlich, z. f. Hyg. 44, 1903, and by Kolle, Chol. Asiat. in Handb. d. Microorg. III, 1903, lit., lit. by Fahr, E. XIII, 1 Abt, 1909, a Kolle, u. Schurmann in Handb. d. path. Mikros. 4, 1912, lit.)

The addition of minute quantities of pure sulphuric acid to a 24 hour peptone-containing bouillon culture develops a violet red color (cholera red). This is due to metabolic products of the vibrios (nitrosoindol reaction), but since it also appears with some other forms of vibrios, it is of no value for differential diagnosis, but of some importance since a

negative result shows that the culture tested cannot be cholera vibrios. Animals are not very susceptible to cholera, but Koch infected rabbits and guinea pigs by immobilizing their intestines with opium, and neutralizing the gastric acid, which kills the bacilli. Pfeiffer also succeeded by intraperitoneal injections of agar cultures suspended in bouillon-saline solution. Vaccination is successful against cholera.

The general activity of the bacilli in the body starts from the intestinal tract where they multiply (incubation time ½ to 2 days), and give up their toxic metabolic products. These toxins may cause after effects even if the bacilli have disappeared.

The course of the disease is divided into: 1st stage, premonitory diarrhea of short duration, 2. the attack of cholera. There are general weakness, chills, dullness, vomiting, singultus, profuse diarrhea, excessive thirst, cyanosis (livid, lead gray), labored respiration, sunken eyes with a translucent brown yellow spot at the lower periphery of the sclera, which is dried and thinned (illustr. by Froriep), sunken abdomen, blue shriveled hands, the so-called washerwoman's hands (p. 780), pulse hardly recognizable (may be reduced to 50 to 40 beats), low temperature (35° to 36°), cholera voice, (Boltz, Stoerk found waxy degeneration in the muscles of the vocal cords), muscle spasms, especially in the calves. The absence of diarrhea is rare, and such cases die in a few hours. Many patients die in this stage (statium algidum), others recover in 1 to 2 weeks. The exanthem consists of small, usually brown red, confluent maculae during convalescence (Arzt). The 3rd stage, typhoid stage, is accompanied by fever and presents a typhoid- or dysentery-like condition; there are bloody, purulent, fetid stools, often with diphtheritic inflammation of other organs (bladder, larynx, etc.), or uremic symptoms from toxic degeneration of the kidneys and anuria.

The anatomic changes in the first and second stages. After opening the scaphoid abdomen, the omentum appears injected, the serosa of the intestines is rose red, dry, and frequently covered with a sticky, delicate coating rich in albumen and feeling like soap in which are desquamated peritoneal lining cells undergoing mucoid degeneration. The loops of the small bowel are filled splashingly, thick and heavy with a peculiar tough feel. The colon is contrasted by its pale gray yellow color. The bowel contents resemble rice water or very thin gruel mixed with white flocculi. When fresh, it has a sweetish stale odor or none at all, and is colorless because no bile is produced; the colored fetid feces have been previously passed, the reaction is alkaline, they contain only traces of albumen, practically no salts but sodium chloride, and a sugar-splitting ferment. The fluid is enormous in quantity and considered to be either a transudate from the capillaries of the mucosa, analogous to pulmonary inflammatory

edema (Stoerk), or, (more recent opinion), a result of hypersecretion of intestinal juice, since the fluid approximates this in its chemical composition. The mucosa is intensively hyperemic, rose red or dark pink with delicate vascular injection, and perhaps punctate or larger ecchymoses. The follicles are swollen and their surroundings actively injected. The mucosa is covered with gray, somewhat thick mucous. Microscopically, the gland epithelium shows considerable mucoid degeneration and necrobiosis (toxin action? Stoerk). In other cases, quickly fatal, the redness is absent, the bowel is pale, gray white, as though water soaked. Later the epithelium becomes detached in large masses.

This highly characteristic epithelial desquamation may be found throughout the whole of the small intestines; examinations made soon after death have shown that it is not a post mortem change as was formerly believed. The fundi of glands are not desquamated during life, nor are whole villi with their connective tissue, but epithelial rags and finger-like epithelial casts appear in the stools. The vibrios are found almost in pure culture in the bowel contents, especially in the flocculae; sections through the bowel wall show them in larger quantities only on the surface and in the crypts, according to Stoerk, never below the basal membrane of the epithelium. Mucosa and submucosa are edematous and more or less infiltrated with small cells.

The feces are mostly free of bacilli in 6 to 8 days after the sensitive stage, but exceptions have been observed (Kolle and others); bacilli were still present 5 to 18 and even 48 days during convalescence.

The chyle vessels in the intestinal walls and villi are filled and swollen; this chyle retention is considered due to impeded circulation.

The colon may remain free, or show swelling and redness of the mucosa, hemorrhages and epithelial necroses above them, developing into shallow ulcers (Stork).

In the third stage the anatomical findings are quite different; sometimes, especially in the uremic form, it might well be called negative. The bowel contents are still liquid, but less abundant, dark in color again and fecal in odor; the colon may even contain formed stools. The mucosa is pale or slate gray, sometimes hemorrhagic. In other cases, especially in the colon, but also in the ileum, there are found discolored diphtheritic scabs, usually of the surface. Deeper ulcers and stenoses are very rare.

### Other Changes in Cadavers Dead of Cholera

Externally the marked cyanosis (gray sombre color) may be striking. Longitudinal folds and twisted wrinkles are present on the fingers (as in washer women). The muscles of the calves at times are as hard as a board. The abdomen is scaphoid. Rigor mortis is early, marked, and of

long duration. In early cases, all the internal organs are hyperemic, in later cases, anemic, dry and pale. The blood is thick, tarry or huckleberry juice-like in color; the clots are poor and loose. The serous cavities are lined with a sticky coating, as on the serosa of the intestines. The kidneys may show signs of severe degeneration (anemic, toxic necrosis of epithelium, cholera nephrosis). Fatty degeneration of the liver and heart, also of the gastric mucosa has been observed. In contradistinction to most acute infectious diseases, the spleen is not enlarged. The hemorrhagic swelling of the uterus (according to Kritzler, infectious or toxic endometritis) may cause pseudomenstrual hemorrhages. For the microscopic cell changes in the cerebral cortex, see Michailow.

**Differential Diagnosis.**—Cholera-like symptoms may be due to acute arsenical poisoning (Virchow) and diabetic coma (Buhl), also and of more practical value to so-called cholera nostra, or vomiting dysentery, the etiology of which is as little known as that of the so-called infantile cholera. (The Finkler-Prior spirillae are of no importance in the etiology of cholera nostra.) In the latter disease it is unnecessary to think of a specific cause; it is sufficient to believe that the higher temperature of summer permits more active increase of the ever-present saprophytes in the milk consumed by children, which produce abnormal decomposition and toxic effects.

**Typhus Abdominalis (Ileo-typhus).**—Generally speaking, several types are differentiated:

Abdominal typhoid fever, simply typhoid, caused by the typhoid bacillus (Eberth-Gaffky). The layman often calls it "nervous fever" on account of the frequent severe nervous disturbances. Toward the end of the first, or the beginning of the second week of the disease, a characteristic exanthem appears on the body, especially on the skin of the abdomen, the rose spots of typhoid, which disappear in 6 to 7 days.

**Exanthematous Typhus.**—Spotted fever, petechial fever, is a severe contagious infectious disease of uncertain etiology, but transmitted through the pediculus vestimenti. Inoculation of the patient's blood causes typical spotted fever in the ape. Increase of this disease to destructive epidemics has been called hunger typhus or war typhus; the mortality to the 20th year, 5%; over 50 years 60 to 70% (Jurgens). The exanthem appears on the 3rd day and is quite extensive, differing from measles, which it somewhat resembles in that it has no eruption on the face. The livid red, macular rose spots may be changed into petechiae by extravasations of blood, but not constantly; indeed, extensive hemorrhagic exanthemata are more suggestive of meningococcus meningitis than of typhus fever (Eug. Fraenkel, Umber, Gruber). As a rule, rose spots are no longer visible on the cadaver, but perhaps petechiae.

Deloused cadavers cannot spread the infection. At autopsy, there is nothing characteristic macroscopically (Nicol), merely the picture of a severe, septic, hemorrhagic general infection. There is parenchymatous degeneration of the glandular organs and the heart; the inflammatory changes of the respiratory tract are secondary infections. Death in the latter stages of the disease is usually due to pneumonia. The meninges and ventricular plexus are hyperemic, and often show small hemorrhages; true meningitis is a secondary complication. Hemorrhages are common in the dark, dry, waxy musculature (Ceelen, lit., Curchmann, Port, Baumler). Microscopically, finding specific typhus fever nodules in the small vessels is especially important, such as were discovered by Eug. Fraenkel in the rose spots (p. 122), and which are found in the small vessels of almost all the internal organs, especially the brain (Herzog, Jaffe). Death in early cases is considered due to this brain change, kidney change, etc. The spleen and lymph nodes show extraordinarily marked phagocytosis of erythrocytes; there are necrosis and disintegration of the nuclei of myelocytes and megakaryocytes in the bone marrow. The question of the cause: the inclusions in erythrocytes, described by Krompecher, Goldzieher and Augyan are probably the same structures earlier described by Gottschlich as blood parasites, not recognized by others (Dreyer); Gottschlich later considered them without specific importance, being only degeneration products of the red blood cells. In the louse which transmits spotted fever, Ricketts, v. Prowazek and others found rods or oval structures with polar staining and central vacuoles. Da Rocha-Lima brought evidence that they are forms of the virus of spotted fever in the louse; he calls the parasites Rickettsia-Prowazeki bodies (both investigators died of spotted fever); the parasite is probably a protozoan. v. Prowazek then found peculiar enclosures in leucocytes of the blood of spotted fever victims, which were also found by Stempell and Hlava in the blood of monkeys, experimentally infected; Ghon considers these of diagnostic importance, with the microscopical examination of excised rose spots (Kyrle and Morawitz). Hauser described the same formations in the vascular foci. Kuczinski considers Rickettsia-Prowazeki the cause of spotted fever, but Eug. Fraenkel is still skeptical. The bacillus found by Plotz-Olitzky-Baehr, bacillus of exanthematous typhus, is not accepted by Gottschlich (lit.).

(Exhaustive lit. by Gottschlich, Munk, Gruber, Herzog, Kamgiesser, Nicol.)

(For the relation of Wolhyn's (5 day fever) fever, to spotted fever, see Jungmann and Kuczinski.)

Typhus recurrent fever is due to the recurrens spirillae (illustr. of spirillae, p. 214) in the blood and organs. There are large splenic tumor

(p. 234), changes in the bone marrow (p. 290), parenchymatous degeneration of the liver, kidneys, heart, and skeletal muscles, etc. (Ponfick and M. Rabinowitsch, lit.).

In spotted fever and relapsing fever the characteristic intestinal symptoms of typhoid fever are absent. For paratyphoid fever, see p. 761. For bilious typhoid, see under Weil's disease.

Abdominal typhoid is an infectious, general disease, due only to the typhoid bacillus; the digestive tract is the portal of entry, from which the organisms pass promptly into the blood stream (bacteremia). It attacks chiefly youthful, robust individuals, and is observed only in humans.

Although individuals of young and middle life are more often the victims, sometimes the disease occurs during the first year of life and even in sucklings (Brelet). The mortality percentage increases with increasing age, but in old individuals, the intestines are usually mildly involved, probably because of senile involution of the lymphatic apparatus. Generally speaking, the mortality is about 11%, but increases to 30% or 40% with advancing age. Typhoid fever in children is relatively benign, anatomically often without ulcers, perhaps only marked by enteritis with follicular and splenic swellings, often masked by a mild clinical picture (sometimes also in adults; Lentz); such cases, remaining untreated, and also persons harboring bacilli without contracting the disease, (carriers), may become a dangerous source of infection, and connecting links in a typhoid epidemic (Koch). But adults in the post-typhoid stage may excrete bacilli for weeks, even months and years (55 years, Martz, lit.) without signs of typhoid fever in themselves or perhaps merely mild digestive disturbances, such as diarrhea or constipation. The bacilli are discharged in the stools (Rost, v. Wiesner) and in the urine, the latter considered more dangerous (Bruckner and lit. by Fromme, Gaehtgens). In these permanent carriers, the gall bladder is the incubator of typhoid bacilli, or the bile ducts or the small bowel (Loele; lit. in appendix; Forster and Kayser, Lemierre et Abrami, Eug. Fraenkel). Although it may be possible to make animals carriers of typhoid bacilli, and even to produce chronic cholecystitis with calculi (s. Emmerich, lit.), the condition, nevertheless, is not an infectious general disease comparable to the typhoid of humans.

In the initial or so-called incubation period of about 10 days in length, or, according to Jochmann, 8 to 14 days, rarely longer, the intestine, especially the ileum, shows acute catarrhal inflammation with sufficient hyperemia to frequently produce small hemorrhages. This diffuse disease of the mucosa, the cause of diarrhea, which may be absent, is added to by localized changes in the intestinal follicles, solitary and agminated, and mesenteric lymph nodes. These typhoid lymphatic changes may also occur in the larynx (p. 318) and nose (rare, p. 293), and in the gall bladder. The spleen

swells; the follicular apparatus of the bowel, after swelling enormously, is reduced, as the disease subsides, by disintegration or emigration of the proliferated cells, or indeed, by a quite definite series of changes. They first become necrotic to varying extent and scabs are formed; by detachment, more correctly, gradual maceration of necrotic portions, the ulcers appear, and after removal of necrotic substances, may heal cleanly and smoothly without scar retraction. The entire process progresses in separate stages which correspond almost perfectly to certain time limits. The changes are especially severe in the lower ileum, including the appendix. The latter, in exceptional cases, may be the only part diseased (Stokes and Amik); but cases occur in which the changes extend high into the jejunum and down into the rectum. If the colon is the chief part involved (rare), it is spoken of as colo-typhoid.

The ulcers come from the disintegration of swollen follicles; they are sometimes innumerable, very closely grouped, rounded, the size of a pea to a half dollar or more. Transverse, sharply marginated ulcers with overhanging edges are also seen. Meteorism causes enormous distension of the transverse colon or the sigmoid, until they are as large as the upper thigh; the contents are foamy, yellow green and turbid like thin gruel; the mucosae are lined with small or large specific ulcers, diphtheritic coatings, nodular abscesses, and the striated ulcers of distension. Multiple perforations are occasionally found. In a peculiar case of meteorism in typhoid, Hitschmann and Lindenthal found an excessive growth of gas-producing butyric acid bacilli, which formed gas bubbles in the deep layers of the intestinal wall, and from there extended into the mesentery.

While the characteristic anatomical lesions are due to the typhoid bacilli and their toxins in the intestines, the severe general symptoms, such as fever, the nervous stages, and also the greater number of the fatal cases, are due to complications (p. 793) from the metabolic products of the bacilli and the bacterial dissemination in the blood stream. (The involvement of the sensory nerves has led to the designation "typhoid" from "smoke," stupefied, giddiness.")

The toxicity may be demonstrated in animals in which, however, the anatomical signs of typhoid have not as yet been reproduced; even sterilized cultures with bacteria removed, retain their toxic properties. In man a typhoid septicemia occurs, the bacilli actually growing in the blood and not merely present passively; there is a positive Widal reaction, but bowel changes are absent (Chiari, Kraus, Lartigau, Flexner, lit., Neufeld, lit., Jores, Posselt, Rehberg). The author saw such a typhoid without intestinal lesions in a 15 year old boy (clinically, rose spots and positive agglutination). Indeed, many consider typhoid a blood disease, a so-called typhoid septicemia, and the intestinal changes merely localizations

of the process. The supposition is that bacteria enter the blood directly from any part of the digestive tract, even from the tonsils (Citron, Oeller; opposed, Graff, etc.), and then localize in the lymph nodes and the lymphatics of the bowel (Beitzke); they reach the lymph nodes first from the digestive tract, and from these the blood (Forster), or the bacilli in the blood enter the liver and from there the bile, or perhaps directly into the gall bladder from the blood, and with the bile reach the small bowel. Others with better judgment believe in a primary infection of the bowel, from which the regional lymph nodes of the mesentery are infected and the blood invaded (bacteremia) (Chiari, Eug. Fraenkel, Marchand). Bayer leaves this question open. In addition, typhoid bacilli occasionally appear in the blood of persons who have no symptoms of typhoid fever (Busse). Recovery from typhoid fever usually confers immunity, probably because the blood serum and tissue juices retain protective chemical substances, defensive bodies, alexines, etc. (Buchner). Typhoid vaccine is used prophylactically (McFarland, Wright); the results are still not statistically valid. The anatomical picture of typhoid fever in individuals who contracted the disease in spite of prophylactic vaccination, is quite the well known ordinary one according to the author's experiences. For serum therapy, see Bessau, and lit. by Gaehtgens.

The serological methods of identification of typhoid bacilli are: Pfeiffer's reaction or bacteriolysis, according to the principles mentioned under cholera; the agglutination test.

According to Gruber and others, the blood serum of typhoid patients or typhoid convalescents or persons recovered from the disease, exerts a deleterious influence on typhoid bacilli even after months. On this fact depends the Widal sero-diagnostic reaction, usually observed after the first week of the disease. To a hanging drop of typhoid culture is added the suspected blood serum; in positive cases, the bacteria, at first very active become immotile and clumped (agglutination). But since every serum, even of the healthy, added in larger quantity has agglutinating properties, the serum tested must be diluted to about 1 in 50 to detect small quantities of the agglutinins. The clumping must be visible under low power; minute clumps visible only with the oil immersion lens, prove nothing. The agglutinated bacilli will regain their motility and can be further cultivated if placed in bouillon. The Widal reaction is of little use in those who have had protective vaccination against typhoid (Grober); previous dysentery-like diseases develop high agglutinin titres (Wolff-Eisener), also infections with bacillus enteritides, (Gardner), with the tubercle bacillus and others (Gaehtgens, lit.).

Typhoid bacilli, discovered by Eberth, and determined by Gaffky to be the actual cause of typhoid fever, are short, broad and plump, but

more slender and frequently in longer threads in the hanging drop showing obvious individual motility. Flagellae at the poles and sides can be made visible by appropriate stains. They do not liquefy gelatin, but form colonies like grape leaves on gelatin plates. They grow in meat bouillon; on potato-discs, they form a membranous coating difficult to see, but easily visible on a platinum wire rubbed across the material and examined with the microscope. As a rule, they do not multiply in water, but remain viable in it for months; desiccated they remain alive for months; thus they are very resistant (sequelae of typhoid, p. 796). Sources of infection are chiefly the feces and urine of typhoid patients and carriers (p. 783), in the former, even in the incubation stage (Conradi); they enter the body on food and in drink. The inhalation of infected dust may also produce infection, but probably not frequently. They remain living for 40 days in room sweepings. The contamination of food may be astoundingly round about. Their demonstration in food and water is both laborious and difficult. Flies may transport the organisms (Klein). (More details by Fromme, 1909, Posselt, 1912, Gaehtgens, 1915.)

They are found in the infiltrations of the bowel and mesenteric lymph nodes, usually in small clumps, lying between the cells; from the spleen they may be grown in pure culture; they also occur in the liver, kidneys, (according to Curschmann, true nephritis develops in only 1%), and in other foci of the disease, thus in the gall bladder (p. 783), etc. They may even multiply in the cadaver. They are excreted in the feces (usually only in the 1st and 2nd week), and in the urine (Raubitschek), even during incubation. They are almost regularly in the blood at some time or other (Curschmann), in the blood of rose spots (especially in fresh spots, Semann), sometimes in the cerebrospinal fluid (Nieter, Silberberg, lit.), but, according to Eug. Fraenkel, very rarely. In microscopic sections, they are sometimes seen as solitary organisms, (occasionally in clumps); the cultural method is superior. (Histology of rose spots by Eug. Fraenkel.) Isolated typhoid bacilli stain easily with Loeffler's methylene blue or carbol fuchsin, and are Gram negative. In sections, they can be stained with dilute carbol fuchsin or Loeffler's methylene blue, etc., 24 hours, wash in water, treat with alcohol, xylol, balsam.

The bacteriological differential diagnosis is difficult between typhoid bacilli and the colon group, regular inhabitants of the bowel. On the media of v. Drigalski-Conradi (litmus-lactose-crystal-violet-agar), the colonies and the media remain blue because alkaline metabolic products are produced, while colon colonies become red because they decompose the sugar into acids. Crystal violet inhibits the growth of colon and paratyphoid bacilli (p. 761) much more than typhoid bacilli. See above, and

Neufeld, lit., Brion, Jurgens, Rolly, Weisskopf, Schweinburg, the complete lit. of Jochmann and Fromme, Gaehtgens, also bacteriological textbooks (v. Baumgarten, etc.).

The bacillus typhi nurium, used to destroy mice, is also pathogenic to man, producing severe gastrointestinal symptoms and even death (Fritzche, lit.).

### Course of the Typical Intestinal Changes in Typhoid Fever

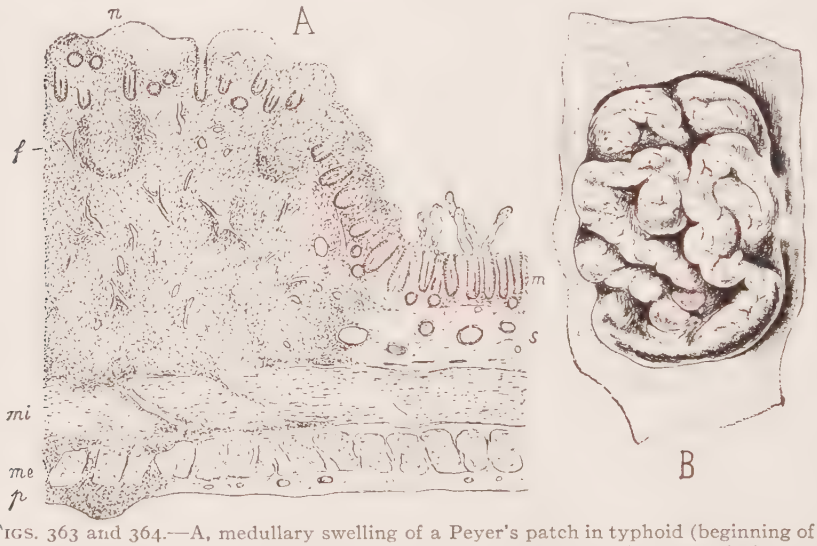
**First Stage.**—Soft swelling (first week to beginning of second week). The solitary follicles, Peyer's patches and the bowel wall swell; follicles normally barely the size of a pin head and often not visible at all become as large as peas or more, stretching and thinning the smoothed mucosa which becomes first red, soft and juicy, but at the height of the swelling, pale and gray. With the marrow-like swelling, there congregate large numbers of peculiar large cells with vesicular, rounded or oval nuclei in the submucosa, with initial hyperemia, and around and near the follicles (the so-called typhoid cells, Rindfleisch). They have a tendency to form nodular foci, and are viewed by Mallory as essential cell elements; they have pronounced phagocytic properties (typhoid phagocytes, Mallory), directed toward lymphocytes injured by typhoid toxin, red blood corpuscles and leucocytes, the latter playing but a small part, and with the nuclei and nuclear fragments in their interior may appear to be multinuclear. Fibrin appears between the cells. These cells, also present in the regional lymph nodes, were formerly called endothelial cells, or endothelial leucocytes; McCallum speaks of mononuclear wandering cells, Graff believes they are histiocytes, *i.e.*, some reticulum endothelium of lymph nodules (local histiocytes), some wandering histiocytes derived from the surrounding connective tissue; active participation of lymphocytes is doubtful. Typhoid bacilli are found in the hyperplastic parts. The swelling also depends on an extension of typhoid granulation tissue to the surroundings, in the depths, as well as on the levels. Cellular infiltration extends lightly to the muscularis and to the serosa (fig. 363). Peyer's patches may appear as lumpy rolls, or wrinkled plateaus resembling cerebral convolutions (fig. 364), or tense elevations with steep margins. They frequently show a fairly even reticular arrangement due to the fact that the follicles which are not enlarged appear sunken in comparison to the swollen interstitial substance of the patches. In the further course, not only the interstitial tissue and the follicles swell more, but Peyer's patches become broader, and longer (12 to 30 cms.) due to the progress of the infiltration in the long axis, causing some patches to coalesce.

The whole ileo-cecal region including the appendix may be involved. The patch adjoining the ileo-cecal valve is circular, while other Peyer's

patches are elongated and opposite the mesenteric attachment. The change is most marked around the valve, often cut short above, or extending with diminishing intensity 1 to 2 cms. upward. The catarrhal mucosa is usually dark red.

The mesenteric lymph nodes, especially the chain draining the ileocecum are swollen, sometimes as large as cherries or walnuts, and contain typhoid bacilli. There is splenic swelling.

In favorable cases, by no means rare, healing may take place from this stage. The cell proliferation stops, involution occurs by migration of




FIGS. 363 and 364.—A, medullary swelling of a Peyer's patch in typhoid (beginning of 2nd week). Margin of a patch (low power); m, mucosa; s, submucosa; mi, int. muscularis; me, ext. muscularis; p. peritoneum; f, a sharply circumscribed follicle, a second to right above; n, beginning scab. (Low power.) B, markedly swollen Peyer's patch with brain convolution design; nat. size.

histiocytes (Graff) or fatty degeneration of cells which are then carried off by the lymph current. The intestinal catarrh disappears. In small children the changes do not often extend beyond this stage of hyperplasia.

### Second Stage

**Necrosis and Scab Formation (Second to Third Week).**—The prominent swollen parts undergo necrosis; the Peyer's patches become encrusted entirely or in part, leaving only an actively injected margin (fig. 365). Scab formation commences with small yellow spots on top of the swollen follicles and patches. By absorption of bile pigments from the feces, the dry, ragged, crumbly scabs are yellow green, brown or otherwise discolored. The scab usually reaches to the musculature, sometimes even through it (danger of perforation). Soft, superficial scabs with subsequent superficial ulceration are rare.

The scab consists microscopically of dead tissue, corresponding to the thin mucosa and submucosa with the follicular and perifollicular cell proliferation established, penetrated by a fibrin network and necrotic blood vessels; the periphery shows a reactive demarkating leucocytic infiltration. The necrosis is considered due to nutritional disturbances from the specific influence of the typhoid bacilli and their toxins. Firmly

FIG. 365.—Marked scab formation in typhoid; two enlarged Peyer's patches with beginning demarkation of scabs at margin. Scab formation over numerous solitary follicles. End of second week; ¾ nat. size.

attached pseudomembranous, fibrinous masses of exudate on the tops of swollen plaques (as emphasized by Marchand, see A. Hoffmann), may be mistaken for scabs. According to Graff, this exudation in some cases is associated with former ulceration caused by detachment of small superficial necroses of mucosa and submucosa. This exudative ulcerative form results from increasing disintegration of the tissue, without the appearance of a leucocytic line of demarkation as in sequestration. But

Marchand considers it improbable that typhoid ulcers form without actual necrosis; the author considers Graeff's classification doubtful.

### Third Stage

**Formation of Ulcers by Detachment of Scabs (Third Week).**— Demarkation begins at the edges and proceeds until the scabs are loosened and detached (by leucocytes). Minute ragged fragments of scab are cast off, maceration sets in, and slow dissolution removes the last particles (fig. 365). Detachment of a scab as a whole by peristalsis probably does not occur; cases which give this impression are probably due to the detachment of fibrinous pseudomembranes, as mentioned above. Thus the typhoid ulcer is oval or rounded, according to its origin from patches

Fig. 366.—Formation of ulcer by detachment of scabs in typhoid; piece of ileum; man 19; $^{9}/_{10}$ nat. size.

or follicles, and usually parallel to the long axis of the bowel. Several irregular ulcers may develop in one patch. The edges are swollen and thrown up, and not rarely somewhat rolled inward. The bases are covered by necrotic masses with depressions and bosses. In many typhoid ulcers the lateral diameter is greater, *i.e.*, the ulcer is transverse; those occasionally appearing above the valve are sometimes immense, occupying the whole circumference of the bowel. When the ulcer enlarges by new swelling and scab formation at the periphery, it is called a lenticular ulcer (fig. 366).

### Fourth Stage

**Cleaning of the Ulcers. Beginning of Healing** (end of third to fourth week).—If no new scab forms after detachment of the old, the ulcer becomes clean by removal of all dead tissue, the base becomes smooth

and the swelling of the periphery is gradually reduced. It usually reaches to or below the deepest layers of the submucosa to the circular musculature which is thus the ulcer base, (fig. 369). Healing proceeds by delicate granulations in the base changing into scar tissue and being covered by epithelium. The scars are delicate, quite smooth, since no follicles are

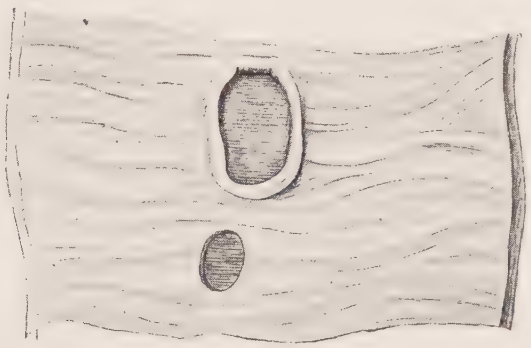


FIG. 367.—Cleansed typhoid ulcers of ileum; the upper with margin still swollen; the lower shows swelling subsided; nat. size.

present, and show no tendency to shrink; they never cause stenosis. In the beginning the area is gray or black, sometimes rimmed with light and slate gray edges. If this pigmentation is exceptionally marked, it may persist for some time. In place of the plaques there remains at times a gray to black stippling (so-called etat pointelle), the dots corresponding

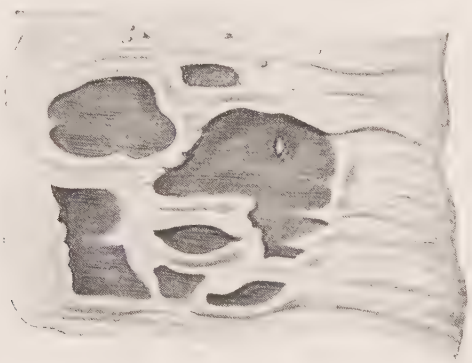


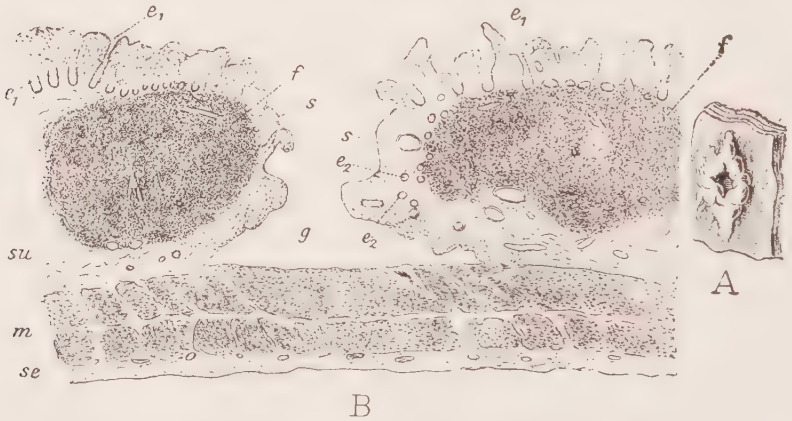
FIG. 368.—Cleansed typhoid intestinal ulcers, thickly grouped, the largest with small slit perforation; 9/10 nat. size.

to hemorrhages in the former follicles. But usually in 1 to 2 months hardly a trace is visible, and in about 4 months the affected areas are recognizable only by their appearing thinner and translucent, due to the destruction of the mucosa including its villi and the submucosa, while the follicular structures may partly regenerate. Relapses occur most frequently in these stages.

The healing process usually begins during the 4th week, and requires 8 to 14 days or more.

The intensity and extent of the intestinal lesions vary much; sometimes there are only a few foci, in other cases, a dozen, 20 to 40; indeed, if the colon is involved, they may be innumerable. In the most severe cases, almost the entire intestinal mucosa is red and swollen, almost poultaceous, and the mesenteric lymph nodes are markedly involved. The several stages are often seen side by side. The most severe changes are near the valve, while the follicles higher up in the bowel are less diseased.

This is usually interpreted as later involvement of the higher parts, but they may just as well be less severely affected throughout the disease.




FIGS. 369 and 370.—A, typhoid relapse. In the vicinity of the cleansed ulcer, in the base of which the muscularis is visible, fresh medullary swelling (5th week of disease); 1/6 size. B, perfectly cleansed small typhoid ulcer; g, ulcer; su, submucosa; m, muscularis; se, serosa; e 1, glands, longit. sect.; e 2, glands, cross sect.; f. follicular patches, still hyperplastic. Alum carmine stain. (Low power.)

The latter is supported by the fact that no matter how far the changes have progressed in the lower ileum, even to perforation of an ulcer in the 5th or 6th week, the upper portion of the small bowel is almost always but slightly diseased.

There are also cases in which recurrence is due to repeated reinfection of the bowel from bacilli in the gall bladder. Then various stages of intestinal changes are found, such as smooth and fresh ulcers, scabs, fresh swelling. Diagnostically, the symptoms, *i.e.*, the fever curve, remain essentially unchanged with no fall and new rise as in a recurrence.

### Atypical Courses. Complication of Typhoid Fever

**Relapses.**—Typhoid may continue longer than usual, because ulcers, already cleaned (4th week) or follicles which escaped or new patches are

infected, swelling starts and the general catarrh again becomes active. The freshly diseased follicles or patches pass through the various changes, and the fever continues for weeks (fig. 369-a). But relapses usually run a shorter and milder course; they occur in about 6 to 8% of cases, the oftener, the lighter the primary disease (v. Hecker-Hirsch). In addition, the frequency of relapses depends on the character of the epidemic. The entrance is marked by increase of fever, swelling of the spleen, and almost always by rose spots, probably also a reappearance of bacteremia (Bennecke, Epstein, etc.). The bowel movements resemble thick pea soup. There are also abortive relapses, characterized by sudden high temperature, quickly subsiding, as in a crisis (Curschmann, Fiedler). A new attack is quite different. In reference to exacerbations, see p. 792.

**Complications during the Course of Typhoid.**—Perforation with subsequent suppurative peritonitis, and the presence of intestinal gases in the abdomen is usually caused by acute exacerbations of the scab formation in the base of an ulcer; it may be accompanied by an increase of fever. The destructive process reduces the bowel wall to a minimum and finally causes necrosis and softening of the serosa. The small holes are often multiple, or the wall tears from peristaltic contractions or the tension of intestinal gases like a hinged box lid. Sometimes a hole the size of a pin head is seen in an ulcer just cleaned (fig. 368). One or more holes may be found, sometimes a big tear due to the confluence of several perforations. Clumsy handling and especially flushing out the bowel contents during autopsy, easily produce artificial perforations. At times a scab with the attached part of the bowel wall may be torn off; such perforations practically always are caused by foreign bodies (fruit seeds). Perforation occurs chiefly in the lower ileum, more rarely in the appendix, cecum or other places. It is evidenced by acute, severe local pain, or sudden generalized tenderness and distension, often especially marked in the upper part of the abdomen; vomiting is common. The catastrophe occurs most frequently in the 3rd to 4th week of the disease; when the course is delayed it occurs later (9th to 10th week). The perforated loop of ileum is usually in the pelvis surrounded by fibrin and pus. Occasionally the peritonitis may be kept localized by adhesions (abdominal abscess). It is remarkable that peritonitis occurs at times without perforation and may even recover spontaneously.

**Hemorrhages.**—If the scab formation and disintegration progress slowly the vessels involved in the necrosis are obliterated as a rule, but if the process is stormy the arterial vessels of the bowel wall are eroded. The resulting hemorrhage may be very severe, up to several litres, indeed, fatal; the blood may escape per anum or remain occult in the bowel lumen; slight hemorrhages are unimportant, but leave pigmentations. Swollen

or scab covered places may be torn by foreign bodies (*e.g.*, fruit stones); this hemorrhage is due to tearing of vessels, and also may be fatal. Hemorrhages are most frequent within the first 10 days or in the 3rd to 5th week; it is often difficult to determine their source.

The hemorrhagic form of typhoid fever is different; a toxic or cachectic hemorrhagic diathesis makes its appearance and at the height or toward the end of the disease; a hemorrhagic exanthem (purpura) of the skin (comp. p. 781, the initial hemorrh. exanthem) and the mucous membranes appears. The prognosis is very unfavorable. (Lit. by Meyer and Neumann, Huber, Caddy and Molony.)

Rupture of necrotic mesenteric lymph nodes (p. 252). Yellow necrotic foci appear in the swollen lymph nodes which contain numerous typhoid bacilli (Levy and Gaethgens); if these foci are demarkated and rupture externally, the result is a suppurative peritonitis (rare). The calcification mentioned on p. 252, is considered by Naegeli more likely due to tuberculosis, which is probably true in the majority of cases.

Suppurative demarkation and abscess formation in a splenic infarct, followed by peritonitis, are rare, (p. 228), but ordinary wedge-shaped infarcts are found at times in the spleen.

In reference to rare perforation of the gall bladder, see under this organ. The bile is usually thin and abundant during typhoid fever. The rupture of a liver abscess is very rare.

**Changes in Other Organs.**– Lymphomas or small nodules composed of lymphoid cells may develop on the serosa over the locally diseased bowel (fig. 363), or scattered in large numbers over the whole peritoneum, or in the liver (see there, also necroses) in the spleen and in the larynx. They must not be mistaken for tubercles. The spleen is always swollen, and Graff believes he can recognize the various stages of typhoid fever from its condition; infarcts and abscesses are not uncommon (p. 229). The respiratory organs are always involved, especially the larynx (p. 314), the nose (catarrh, hemorrhages) and the bronchi. Likewise the upper digestive tract, the palate, tonsils, base of the tongue, etc., may participate, and even ulcerate (lit. by Posselt).

Sometimes a pneumonia precedes typhoid fever and the bowel is secondarily involved (pneumotyphoid, Gerhardt); in other cases, a croupous or focal pneumonia is added to ileo-typhoid. (For typhoid bacilli in the sputum, see Jehle, lit.) Typhoid patients not rarely die of hypostatic pneumonia which follows degeneration of the respiratory muscles. The muscles in general, especially the abdominal recti, abductors of the thigh, diaphragm, often show the waxy degeneration of Zenker, become spotted or striated, or diffusely pale, wax gray or yellow to white, dull, fragile; other muscles appear like smoked meat, red and dry. The fatty degenera-

tion is probably due to toxins. Not rarely the muscle tears and hemorrhages (hematoma) occur in the rectus abdominalis. Later the muscle is regenerated (see under chapter, muscles).

The heart muscle, kidneys, liver show various degenerations such as cloudy swelling, fatty degeneration, necrosis. Thrombosis in the veins of the leg is not rare (p. 153); it may lead to fatal embolism; among other causes, one is weakness of the heart. The author is of the opinion that bacteremia might be of importance. Decubitus, often very extensive, is also considered due to a weak heart.

Necroses which sometimes appear in peripheral parts, such as the phalanges, toes, tip of nose, ears, are perhaps due to embolism or thrombosis; according to Biron, those in the extremities are more probably due to arteritis. In reference to the bone marrow, see p. 290. Meningitis due to typhoid is rare. Curschmann has shown that typhoid may begin with pronounced symptoms of cerebrospinal irritation which, however, are soon replaced by the usual symptoms. In such cases, Loeb believes the primary typhoid infection is in the meninges, starting from the buccal cavity; he also thinks that the so-called "pseudomeningitis" in typhoid fever is true meningitis in many cases, usually of the type of acute serous meningitis. Typhoid bacilli have been demonstrated but rarely by lumbar puncture. Others believe pure toxic action is the essential factor (see Staubli, typhoid meningismus). But there does occur a typhoid suppurative meningitis (Staubli) and a very rare typhoid brain abscess (Posselt, lit.). Cerebellar changes are described by Spielmeyer, as a glious thickening consisting of large, long drawn out, glia elements rich in protoplasm and characterized by numerous mitoses. For participation of the spinal cord (typhoid encephalomyelomeningitis), see literature by H. A. Muller.

Typhoid orchitis is rare. Typhoid cholecystitis with palpable enlargement of the gall bladder (Chiari), on the other hand, is quite common. Indeed, Forster and Kaiser view the gall bladder as an incubator of typhoid bacilli, from which they are spurted into the bowel; according to Chiari, this is the cause of some relapses (cf. p. 792 for reimplantation). The organisms may pass from the blood into the liver, thus into the bile and with it to the gall bladder; perhaps, they may enter the wall of the gall bladder directly from the blood stream (J. Koch, Chiarolanza, Quenu, lit., p. 783). This may cause an actual infection of the gall bladder but the organ itself is often not diseased even though the bile contains bacilli (Hirsch, Eug. Fraenkel). On the other hand, no previous symptoms of typhoid fever may be present, and yet a primary typhoid cholecystitis can be found (Posselt and comp. p. 783). Liver abscesses are very rare (Swain); and still more rarely, they contain typhoid bacilli (Melchior, Adelheim, lit.).

### Diseases Which Accompany Typhoid Fever and Which Follow It

It is important to know that typhoid suppuration may appear during, or in conjunction with, or long after typhoid fever. While virulent typhoid bacilli do not induce leucocytic reaction, the avirulent types produce a leucocytosis (Hess, Adelheim, lit). These abscesses appear in the spleen, liver, thyroid, etc., and various forms of suppuration occur in serous membranes (peritoneum, pleura, meninges); suppurative otitis media and suppuration of cysts of the ovary have been observed (see Werth, 8 months after typhoid, lit. by Gans, Kriwsky). But most important are the conditions in the osseous system, such as periostitis, ostitis, osteomyelitis, chiefly in youthful individuals, and polyarticular, serous, pyemic, or monoarticular purulent arthridites. The tibia is the bone involved most frequently, then the femur; these conditions may accompany the typhoid fever or make their appearance months, or even years after recovery (more details under bones).

**Intestinal Tuberculosis.**—Tuberculosis is the most frequent specific infectious disease of the bowel. Tubercle bacilli may reach the intestines with the food and produce a primary tuberculosis which may remain confined to the intestine (primary isolated intestinal tuberculosis). The organisms are ordinary tubercle bacilli, and also those of animal tuberculosis (bovine tubercle bacilli, see p. 489), as transmitted by milk and the butter from tuberculous cows, sheep and goats, not merely as Ostertag and others assume, from the udders alone, but also from the flesh of the animals (as also the pig); in spite of the protective vaccination of v. Behring, tuberculosis of animals, especially of cattle, does not seem to diminish (Eber). Primary intestinal tuberculosis is decidedly not as rare as was formerly assumed; Heller and others (lit. in appendix) found it quite often (percentage data by Beitzke); Bonome in 24% of children up to the 15th year. On the other hand, others saw it less frequently, thus Albrecht in less than 1%. These differences are probably due in part to autopsy methods or in part to the consumption of boiled or unboiled milk. Finally, the intestines are not rarely the portal of entry if the cases are considered in which they pass through the intestinal wall without injuring it, and in which the bacilli are harbored in the mesenteric lymph nodes (as in animal experiments by Bartel and others, disputed by Takeya and Dold, lit.). Tuberculosis localized in the lymph nodes leaves a cheesy, chalky focus. The ileo-cecal region is favored and so-called surgical tuberculosis of the mesenteric lymph nodes can be diagnosed by the presence of a tumor (Gehrels). It also happens that but a single intestinal ulcer is developed which heals, but not its secondary focus in a lymph nodule. It is not improbable that such cases, mostly children, are infected by the organism of bovine tuberculosis, or at least one which is less pathogenic for man (lit. Hess); but it is

doubtful whether the bacillus of bovine tuberculosis is satisfied, as a rule, to produce such relatively harmless infections in man, confined to the portal of entry and its related nodes or merely to the latter. According to the investigations of Fibiger, Jensen, Bonome and others, it is quite doubtful. But primary intestinal infection is considerably less important than primary aerogenous pulmonary tuberculosis according to most pathologists and many hygienists, especially Flugge and his school, in contradistinction to v. Behring's teaching which regards the milk of tuberculous cows as the chief source of danger (see Kossel, Weber). Both forms of infection may be present in one individual, and on the other hand, it has been demonstrated that pulmonary tuberculosis may develop from primary intestinal tuberculosis by hematogenous routes (p. 433), (see Kovacz and others, lit. by Furst, and in appendix) and in other instances, autoinfection from ulcerative pulmonary phthisis may produce intestinal tuberculosis from swallowed tuberculous sputum. This type of secondary intestinal tuberculosis is far more frequent, and is found in about 90% of cases of pulmonary phthisis, although less frequent in tuberculous children; it is not rare in ulcerative pulmonary tuberculosis, even though usually of less extent; however, under just such conditions the author has often seen quite extensive ulceration in the bowel. Tuberculous ulcers by liberating fragments containing tubercle bacilli may start new infections in lower segments. Intestinal ulcers may also come from retrograde extension from a mesenteric lymph node (Edens). More frequently, however, infection takes place from a fistulous rupture into the bowel of caseous lymph nodes, especially in the ileo-cecal region (consult under "tubes," rupture of tuberculosis of the adnexa into the rectum). It must also be taken into consideration that tubercle bacilli may reach the bowel through the bile and produce secondary intestinal tuberculosis in this way, because animal experiments have shown that the intravenous injection of tubercle bacilli is followed in many cases by their appearance in the bile (older investigations and more recently L. Robinowitsch; also Joest, who found rupture of pericholangitic tubercles into the bile channels, see under liver). Intestinal tuberculosis like typhoid fever is preferably localized to the follicles and Peyer's patches; thus, favorite sites are in the lower ileum and the region of the ileocecal valve where most of the follicles are located. The formation of ulcers may nevertheless extend up as far as the duodenum and even to the stomach, and down as far as the rectum. Cases have been observed in which the ileum was quite free, the process expending its energy in the colon and rectum.

Early infections of Peyer's patches and solitary follicles appear as nodular elevations the size of a millet-seed or half a pea. They are at first gray and cloudy, later yellowish, opaque and caseous, until the whole

nodule is caseous. They then soften, the mucosa ulcerates, the soft caseous masses escape; a rounded depression, the primary (tuberculous) caseous follicular ulcer is the result. They should be found first in the ileum. They are crateriform, at first have only a small central defect (as large as a pinhead, have swollen caseous edges and caseous bases). Neighboring ulcers often coalesce. They resemble follicular abscesses (see p. 764).

Microscopically, characteristic tubercles with epithelioid and giant cells are found in the freshly swollen follicles, or diffuse caseous inflammations parallel to caseous pneumonia. Bacilli can be found in the very beginning of these changes. See Leupold in reference to inflammatory changes in the plexus of Auerbach which may explain the diarrhea of intestinal tuberculosis.

Perhaps less frequently, but often combined with caseous folliculitis, the first changes are miliary or submiliary tubercles (2) isolated, or in groups in the mucosa, submucosa and muscularis. They are usually surrounded by a red halo and are sometimes directly in the edges of follicles. Disintegration of these nodules produces small cup-shaped ulcers, true primary tuberculous ulcers in the anatomical sense, which enlarge and become deeper by confluence and by extension peripherally and into the depths. During their further progress, the caseous follicular ulcers behave in quite similar manner.

Miliary or submiliary tubercles then develop in the bases and margins of the primary ulcers thus producing the secondary tuberculous ulcers with angular margins (fig. 371).

It is a peculiarity of the tuberculous ulcer that its base becomes thicker as it becomes deeper because ever new miliary tubercles are closely massed together in the base and margins. For this reason perforations are quite rare notwithstanding the frequency of the disease.

By confluence of adjoining ulcers an eroded area as large as a dinner plate is developed often plainly circular or annular. Some may be a foot long. Sometimes the structures become gangrenous and diphtheritic inflammation develops in the lower segment, as though the secretions of the large ulcer had corroded the mucosa, (according to Sikl, this may be due to implantation of dysentery bacilli). The intestinal wall may become markedly thickened.

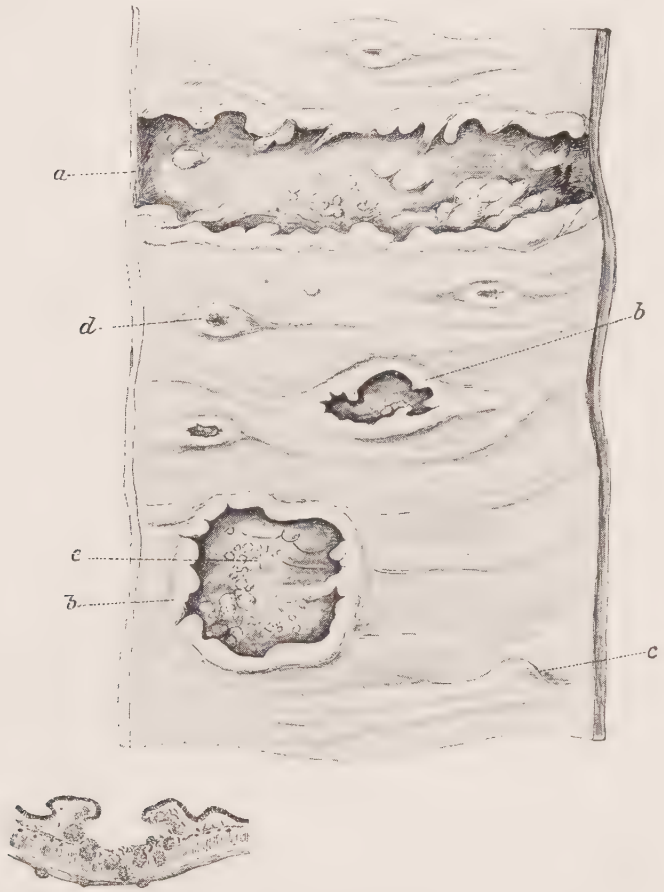
**The characteristics of older tuberculous ulcers are** (fig. 371): (*a*) They are usually at right angles to the long axis of the bowel with a tendency to become annular corresponding to the lymph vessels.

(*b*) The edges are scalloped, very irregular, undermined and heaved upward. Tubercles are seen in the thickened, infiltrated wall.

(*c*) Recent ulcers have diffusely caseous bases or gray and yellow nodules which on cross section may extend into the muscularis to the serosa

(fig. 371). The bases of older ulcers are covered with gray or gray red granulation filled with tubercles; the walls are thick. Even if no nodules can be seen with the naked eye, the base always contains microscopic tubercles which may be disseminated far into the muscularis and serosa.

Isolated polypoid islands of mucosa may persist in the midst of very large ulcers produced by confluence of adjoining smaller ulcers.




FIGS. 371 and 372.—Tuberculous ulceration of bowel; a, older annular ulcer; b, smaller older ulcers with pronged borders and undermined thrown-up margins; c, caseation of a follicle; d, caseous follicular ulcer; above it three slightly swollen follicles; ¾ nat. size. The small figure shows a cross section through a tuberculous ulcer in the vicinity of which tubercles extend through the muscularis to the serosa. Nat. size.

The granulating bases even if they still contain tuberculous tissue may be covered from the edges by cylindrical epithelium in one or several layers; indeed glands of Lieberkuhn may develop, occasionally also cysts, adenomatous proliferations, branching gland ducts (amenomiya), but this should not be spoken of as healing if a trace of tuberculous tissue remains; it is only epithelialization or surface repair.

(*d*) Tubercles are seen frequently on the serosa over the ulcer as dark blue gray vascular dots or as felted, finely villous proliferations covered with vessels. The tubercles follow the lymphatics like a rosary or string of pearls, or in stellate figures along the long axis of the bowel, or across the bowel toward the mesentery where they may be followed to a lymph node, usually near the mesenteric attachment. Adhesions are common between adjoining loops of intestine and the omentum. But involvement of the mesenteric lymph nodes is usually slight if the ulcers, even though numerous, are secondary to pulmonary phthisis.

**Consequences of Ulcers.**—Cicatrization—stenosis. Complete healing with disappearance of all tubercles and purely cicatricial change of the granulation tissue is somewhat rare and if the ulcers were deep and circular,

FIG. 373.—Hyperplastic cicatricial tuberculosis of cecum; area of granular papillary ulcers and polypoid excrescences; woman 26 years old, phthisical; ¾ nat. size.

marked stenosis with possible intestinal obstruction always results. The reaction is very marked on account of the massive development of granulation tissue in the bowel wall. The scars are dark gray in color and may be mistaken for the much rarer syphilitic scars (Fibiger). But stenosis may also occur in incomplete healing. There is marked dilatation and hypertrophy above, so that a dilated segment of small bowel may resemble the colon. In a case observed by the author, the circumference of the small bowel below a stenosing ulcer was 5.5. cm., above it was 19 cm. and this is not at all unusual.

In a not inconsiderable number of cases even in children (lit. in appendix), the stenoses, almost exclusively in the ileum, are multiple, partly ulcerative, partly (rarer) cicatricial, some showing polypoid excrescences; (the author counted sixteen in one case). The intervening segments may be spindle-shaped and have thickened walls. There may be entire freedom from adhesions. In the ileocecal region, especially in the cecum, more

rarely elsewhere in the colon (splenic flexure, see p. 802; ascending colon, Kuttner), but also sometimes in the ileum (see above), there develops a stenosing, hyperplastic, cicatricial tuberculosis which may be mistaken for a neoplasm, *i.e.*, carcinoma (according to Kuttner a neoplasm may also resemble tuberculosis; lit. in appendix). Other forms are like fungi, others resemble diffuse infiltrating and stenosing carcinomata. (Good illustrations by Hartman.) In still other cases the mucosa is papillary at or near the narrow area from connective tissue proliferations or villous polypoid mucosa remains. According to the author's experience (5 more recent observations in boy 8 years and females aged 19, 26, 46, 50 years), this is the most frequent form. Typical tuberculous ulcers may be alongside. In the majority of cases quite analogous to the tuberculous stenoses of the small intestines, the changes are characterized by marked connective tissue proliferations with tubercles and ulcers in various stages of disintegration or healing. The author has observed that characteristic tuberculous changes may be confined histologically to a few nodules. There are also exceptional cases in which the hyperplastic cicatricial tuberculosis involves large areas of the colon without causing noteworthy stenosis thus resembling old ulcerations of dysentery (fig. 373). Richter (lit.) believes it probable that a non-specific, chronic, ulcerative inflammation of the submucosa with abscesses, fistulae and scar tissue is the chief cause in such cases, while the tuberculosis is more of the nature of an accidental infection. Sometimes stenosis is caused by cicatricial contraction from without as, for instance, from granulation tissue on the outside of an old ulcer.

*Perforation*, generally speaking, is rare (cf. Berard et Patel) and occurs only in acute annular ulcers which undergo quick caseation. The opening is circular, sharply cut, and usually small; if it communicates with the abdominal cavity it leads to general suppurative perforative peritonitis. The perforated loop is usually in the lowest part of the pelvis if of the ileum, which is most frequently the case. Sometimes the perforations are multiple as in the puerperium of twins born in the seventh month (author). The appendix which is very often involved is also occasionally perforated. During the autopsy it is advisable to investigate first the ileo-cecal region carefully and if nothing is found, to lift out the loop which lies deepest in the pelvis. It is astonishing how frequently the perforation is found in this situation.

In old ulcers the thickening of the serosa usually protects from perforation. If perforation occurs into an already encapsulated space, an encapsulated fecal peritonitis results. Adjacent loops bound together by adhesions may communicate by fistulae due to perforation of ulcers (bimucous fistulae).

Sometimes an ulcer perforates into an adjacent organ, *e.g.*, the bladder, or into the stomach from a stenosing ulcer of the splenic flexure (very rare) through an abscess cavity and fistulae (see Thorspecken), or as in a case published by the author, from the ileum into the uterus. Rupture into the retroperitoneal tissue causes phlegmons which sometimes perforate the skin as a fecal fistula. Rectal and anal fistulae develop by perforation from the rectum into the periproctal tissue (see under rectum, p. 842).

Hemorrhages are frequent, but they rarely endanger life.

General tuberculosis of the peritoneum is another possibility.

Carcinoma may develop in the base of old, partly cicatricized tuberculous ulcers, or in hyperplastic tuberculous tissue. Herzog described two separate growths from two old ulcers distant from each other. The carcinoma may spread diffusely over the ulcer. Lymph nodes may be both carcinomatous and tuberculous.

**Syphilis of the Intestines.**—Syphilis of the intestine is congenital or acquired; the latter is very rare and the congenital form is always part of other syphilitic changes (lungs, bones, etc.), and is infrequent. Chiefly in the small intestine, especially in the ileum, rarely in the colon, there appear multiple, bacony, gummatous plaques which disintegrate to ulcers resembling those of tuberculosis, but usually less deep. The base is bacony and fibrous. They may be encircling and stenosing.

The gummas lie either within or without Peyer's patches. Peritonitis above the area is not rare; even perforation has been observed (very rare) (Kundrat and Mracek). Miliary gummas also occur (lit. by Oberndorfer). Spirochetae have been found in isolated cases (Warstat, lit.).

In acquired syphilis (2) localization in the small intestine is very rare (lit. by Gutmann and Eug. Fraenkel). It prefers the upper segments (in contradistinction to tuberculosis), producing lumpy, nodular elevations from which flat smooth ulcers arise; stenosis is rare. Eug. Fraenkel saw death from hemorrhage from an artery in the base of a gummatous ulcer. The ulcers occur in the colon (flexures, but chiefly the rectum), probably seldom as primary wounds, but in the late stages from disintegration of gummas in the mucosa and submucosa. The gummas are first flat, red elevations (histological perivascular round and spindle cell foci, panarteritis and panphlebitis), but soon disintegrate superficially to flat, sharply demarkated ulcers with smooth, bacony, yellow or gray bases. The infiltrations and ulcers show a tendency at times to become ring shaped like carcinomatous ulcers, and their marked tendency to cicatrize leads to stenosis; a carcinomatous ulcer usually has rolled up hard margins and a broken up base. The smooth syphilitic ulcer resembles more a healing typhoid ulcer. According to Fibriger, most so-called syphilitic scars of

the small intestine are probably of tuberculous origin. Perforation is frequent.

See Goto, lit. for syphilis of the ileocecal region; for syphilis of the rectum, see under "chronic ulcerative proctitis" (p. 842).

See Horn (lit.) for primary chancres of the anus (usually from anal coitus).

**Actinomycosis.**—Actinomyces may reach the intestine in vegetable and other foreign bodies (Bostroem, Brunner, Schumann) and produce white plaques of primary fungus growth (Chiari), or mucus, especially submucous, nodular infiltrations, which undergo suppuration and become shallow ulcers. It is most frequent in the colon, chiefly the cecum. Numerous branching fistulae from the ulcers lead to adhesions of loops of bowel, abdominal collections, and larger fecal abscesses in the retroperitoneal tissues. These have sulphur yellow, friable walls. Abundant cicatricial tissue is drilled by fistulae and abscesses. Thus the organs, especially of the pelvis (bladder, genitalia) are completely enveloped. But perforations into hollow organs are often multiple, thus into the intestine, or into the pleural cavity, or along the ileopsoas muscle into the thigh. Eventually, perforation occurs through the abdominal wall, or, as the author saw, even into the hip joint. Aggregations of fungi are found in the pus (p. 467), sometimes stained brown by bile pigment. The course may be very chronic (Herz, lit., Harbitz and Grondahl).

There are also cases with stenosis, others with neoplastic extramural actinomycomas (Brunner).

Sometimes it gives symptoms of appendicitis (p. 834) and peritonitis, circumscribed at first (see p. 842, actinomycotic proctitis and periproctitis).

In these cases, metastasis to the liver is rather frequent (see illustr. under liver).

H. Burckhardt saw a combination with carcinoma of the colon. See Beyerlein in conjunction with tuberculosis.

Secondary actinomycosis of the abdomen may follow actinomycosis of the pleural cavity (p. 469).

The other main channels by which actinomyces enter the body are the mouth and lungs (pp. 557 and 466, also under skin).

**Intestinal Anthrax.**—Primary anthrax develops from the ingestion of meat or food infected with the bacilli; secondary intestinal anthrax occurs when, *e.g.*, the portal of entry is the skin and the distribution is via the blood stream. The gastric and intestinal mucosa, especially that of the small bowel is hyperemic and hemorrhagic. The hemorrhagic foci like boils produce internal elevations, appearing red through the translucent serosa. They show central scab formation similar to the furuncles and carbuncles of the skin, then become brown red and disintegrate into

moderate sized ulcers. Sometimes the ulcers select the top of the folds and are then transverse. The bacilli are present in the foci in enormous numbers. The mesentery, the omentum, and the retroperitoneal tissue, may become gelatinous and edematous. The lymph nodes are congested and hemorrhagic. The author has observed edema of the abdominal walls and sero-purulent ascites.

### Atrophy and Degeneration

Degenerative atrophy and disappearance of the glands, especially those of the colon are frequent (post mortem maceration?); sometimes inflammations precede the processes.

The muscularis may simply atrophy, or the cells contain brown granules (brown atrophy). Macroscopically, the thin muscularis as a whole appears rusty to deep brown (intestine of alcoholics). At times there is also pigmentation of the liver (with cirrhosis), of the pancreas, lymph nodes, etc., (hemochromatosis). According to v. Recklinghausen, the brown pigment in the intestinal musculature is iron-free hemofuscin.

In hemochromatosis, the pigment in the other organs is chiefly iron-containing. Hemofuscin contains sulphur and, according to the opinion of many, belongs to the melanins which are probably derived from proteins (Rosenfeld); Hueck considers it a lipofuscin, *i.e.*, a catabolic pigment from lipoid substances (p. 49).

Melanosis of the intestinal mucosa is the designation given to a dark brown to black discoloration of the mucosa, especially, and sometimes exclusively, of the colon, including the appendix (Solger, Pick). At times the lowest segment of the ileum is involved, as in a 78 year old, extremely cachectic male, with deep black brown mucosa of the colon uniformly dark except where the lymph nodules were recognized as brighter spots. In less severe cases, the mucosa shows a peculiar dark pattern (like alligator skin, Pick). The amorphous, iron-free, acid-fast pigment is deposited in the connective tissue cells of the mucosa, according to Pick, but according to Henschen and Bergstrand, in its "wandering cells;" gland epithelium and lymph nodules remain free. Flat sections through the mucosa are very instructive; a brown network is revealed each mesh of which contains a gland if it has not fallen out (scissor sections from fresh material). Pick thinks the pigment is derived from colorless aromatic protein catabolic products (indol, skatol) which are absorbed into the mucosa from the intestinal contents to become changed to pigment by a fermentative process (assisted by a tryinase?), but according to Hueck, it is possible that colorless pro-pigments derived from lymph and blood can reach the mucosa by excretion and then become oxidized into pigments. The chemical nature of the pigment is under dispute (true

melanin—Pick; related to the lipofuscins—Hueck; different from both, requiring a special place—Henschen and Bergstrand). Severe characteristic stages of melanosis of the colon are rare; lighter degrees are frequent; sometimes a chronic disturbance of function (chronic constipation) seems to play an important part. But the factors causing its development are still an open question (cf. Henschen and Bergstrand, lit.; Fibiger). To speak of ochronosis of the colon (Orth) is inadvisable since ochronosis is a well defined disease (see under cartilage) in which the bowel is not involved in the pigmentation.

See p. 759 for so-called villous melanosis and nodular pseudomelanosis; also see p. 659.

According to Nothnagel, the musculature may be congenitally weak, and degeneration is frequently found in phthisics, alcoholics, very old people and in chronic peritonitis.

The teaching of intestinal atrophy is based chiefly on the statements of Nothnagel who found atrophy in 80% of bodies. This conception is much disturbed by the investigations of Gerlach who emphasized the importance of post mortem gas distention in the thinning of the intestinal wall. Heubner and Habel, and especially Taber and Block, describe the changes which develop in the putrefying bowel of the cadaver. For the same reasons, the latter authors doubt the presence of an (gastric) intestinal atrophy in pernicious anemia (Ewald, Eisenjohr, Koch, Martius, and others).

Amyloid degeneration involves the blood vessels (arteries and capillaries) as well as the connective tissue apparatus of the mucosa (especially the villi), the submucosa and the muscularis. The ileum is the part most frequently diseased. Lymph follicles and patches remain free as a rule. The ileum is pale and glassy; the colon is also pale and glassy, sometimes stiffened, swollen, or is spotted or diffusely gray to gray black in color. Sometimes there are no macroscopic lesions. Amyloid of the intestine is found, among other conditions, in phthisis and syphilis, usually with amyloid of other organs (spleen, liver, kidneys). In a case of multiple myeloma, Askanazy saw local nodular amyloid in the intestinal musculature.

**Amyloid Reaction.**—If Lugol's solution is placed on a pale area of the mucosa and washed off with water, brown vascular branchings, dots and striae appear. According to Orth, it is best to treat the part covered with iodine, with acetic acid to prevent bleaching of the iodine by a possible alkaline reaction.

**Hyperplastic Conditions and Tumors of the Intestines.**—In leucemia, especially the acute forms, and also in aleucemic adeny (pseudoleucemia, see Hoffmann, and p. 205) there are sometimes observed quite enormous

thickening of follicles and plaques, and extensive proliferation of the adenoid, mucous and submucous tissues. These develop into immense button-like follicles, giant patches and tumor-like bulgings, lumpy and convoluted, with stretched, smooth surfaces, which on section, are white red and glassy. The cecum and appendix are frequently involved. The mesenteric lymph nodes may reach the size of a child's head. Leucemic intestinal tumors may show surface necrosis. In the acute leucemias are added severe hemorrhagic infiltrations and necroses (cf. Marchand). Without examination of the blood, mistakes for primary malignant tumors are possible. In lymphogranulomatosis (p. 267) there appear (rare) extensive infiltrations and deep ulcerations, either isolated in the bowel (and stomach) without involvement of lymph nodes (Schlagenhaufer), or by continuity from lymphogranulomatous lymph nodes (Hauck). There is a resemblance to typhoid fever when the leucemic infiltrations are less voluminous, ulcerated, and localized to the patches and follicles of the ileum (Herxheimer, lit.).

## True Tumors

**Benign Tumors.**—Fibromas are very rare (Stetter, lit.) apart from the polypoid fibromas of the lower rectum (p. 814). Myomas (and fibromyomas) springing from the musculature of the small bowel and colon are rather rare and not large as a rule; they may be differentiated into internal, in the lumen, and external varieties; the latter are sometimes very large, exceptionally, as large as a man's head and up to 6 kilos in weight (Lorguet, Steiner, lit., Lieblein). In a boy 7½ years old, the author saw invagination from a fibroma of the ileum the size of a cherry. They also occur in the rectum (Lexer, Becker, Linsmayer). Literature by Hake, Hauswirth.

Adenomyomas are occasionally met in the duodenum and jejunum; they are small and polypoid, and are supposed to be related to an accessory pancreas (Trappe, Weishaupt, lit.), or to misplacement of intestinal mucosa, also to enterocystomas, or, as in the case of Verse (lit.), to rests of the omphalomesenteric duct (Thorel).

Josselin de Jong (lit.) described subserous adenomyomatosis of the small bowel extending into the muscularis and causing intestinal stenosis; he considered it due to proliferation of the epithelium of the serosa. Gland ducts with cylindrical epithelium are imbedded in cellular tissue; this is surrounded by a coating of muscle cells, derived from the longitudinal muscle. Inflammatory changes are absent. In a 53 year old woman, the author saw an adenomyosis of the sigmoid causing tumor-like thickening and narrowing in two places (operation for ileus and suspected carcinoma).

Lipomas, as lobulated nodules in the submucosa (internal lipomas), may push the mucosa ahead, and develop into very long pendulous polyps (figs. 374 and 375). Rarely they reach the size of a hen's egg or fist, but frequently cause invaginations (Hiller, Andree, lit.). Removal by the natural route is rare (cf. Kothny). They are found chiefly in the colon; obese individuals are favored. This is especially true of subserous lipomas (external lipomas) most of which are lipomatous epiploic appendages becoming as large as pears or even fists (Ehrlich, lit. Hengstenberg. Fromp, Schneller, Voeckler).

FIG. 374.—Pendulous, polypoid submucous lipomas of colon; the left, from the transverse colon of a woman of 72; the right in the ascending colon of woman of 62; ½ nat. size.

When the epiploic appendages of a whole region become enormously rich in fat, as in fig. 375, the condition should be classed with the hyperplasias but is spoken of as lipomatosis, usually a part of general adiposity. Hemangiomas are usually cavernous, small, flat and rather rare. Tuffier saw hemorrhages and severe anemia. Kausch saw a rare diffuse cavernous angioma of the whole rectum which pushed into the periproctal tissue (patient 16½ years old, had been operated on as a child). In a 32 year old man, the author saw a diffuse hyperplastic angioma of the cecum which, starting from the submucosa, where it was well developed, spread through the markedly hyperplastic muscularis to the serosa, and somewhat into the mucosa. The area occupied by the angioma, about 8 cm. wide by 8 cm. long, bulged into the lumen while the outside of the intestine

was correspondingly deep and inverted; the proximal part of the appendix was also pulled inward. This inversion, or beginning invagination had caused intestinal obstruction.

Lymphangiomas are very rare; the author saw a cystic lymphangioma the size of a walnut situated in the submucosa of the anterior wall of the rectum. For multiple small neurofibromas (or neurinomas), see under stomach, p. 691.

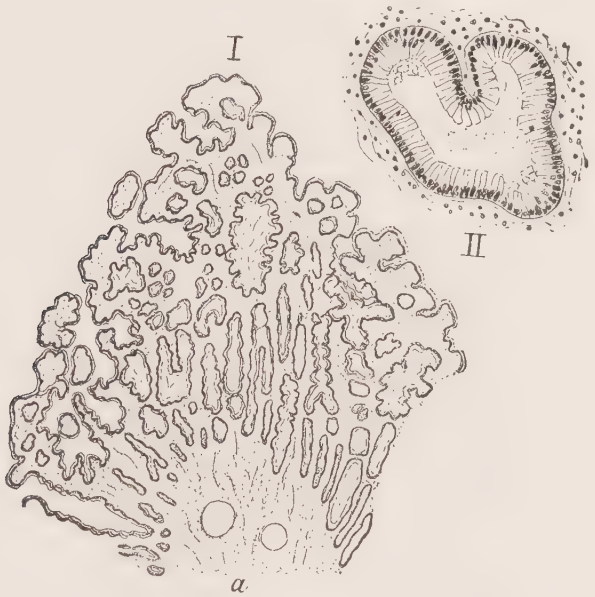
FIG. 375.—Marked lipomatosis of the epiploic appendages of the sigmoid; from a woman, singer, obese, 59 years old; ¾ nat. size.

Adenomas, polypoid or papillary (villous), are rather frequent. Proliferation of glands is essential in their production. The submucosa is passively pulled upward, or actively participates in the proliferation, supplying a fibrous core, often very cellular and vascular (fibroadenoma papillare, fig. 376).

These tumors are usually multiple and small, but occasionally as large as a fist or more. They may produce invagination (especially in the small bowel) or obstruction or prolapsus, in which latter case the tumor itself may protrude first from the anus.

The newly formed glands lined by a single layer of cylindrical epithelium are simple or branched cylindrical epithelial tubes, often cystically dilated; the cells are large, markedly chromatic and often filled with mucus (goblet cells). In contradistinction to cylindrical cell carcinoma, with which they have some similarity (fig. 305), the adenomas do not transgress the borders of the mucosa.

Large papillary adenomas (fig. 378), single or multiple, and as large as a fist or more, grow mostly in the colons, especially the rectums of young individuals and children. They often bleed, cause stenosis by




FIGS. 376 and 377.—From a cauliflower-like papillary fibroadenoma as large as a fist of the rectum of a boy. I. (Med. magn.); a, submucosa. II. Cylindrical epithelial tube. (High power.)

invagination, protrude from the anus and become gangrenous. For these reasons they are clinically fairly malignant.

Various pictures result from numerous polypoid adenomas (intestinal adenomatous polyposis). (1) They may be innumerable, closely approximated, small, fairly uniform in size, slightly pedunculated or almost like nodules in the mucosa which is otherwise intact. They may grow throughout the whole intestines from the pylorus to the anus, equally distributed. The author has observed coincident gastric polyposis in such a case (see fig. 380). Another case of this type occurred with carcinoma of the rectum (in a 37 year old woman). (2) Other cases show variously shaped polypoid adenomas, often with long pedicles, and usually larger, up to the size of a walnut, but much less numerous. Gastric

polyps and intestinal carcinoma are also frequently coincident; it is easy to believe that the latter developed from a polypoid adenoma, see Hauser, Verse, but according to Ribbert, carcinoma does not develop from a polyp, but on one, especially because of cases in which several carcinomatous polyps are present (Weichselbaum, Doering). In one such interesting case, investigated by the author, (68 year old man) two adenocarcinomas the size of cherries and one the size of a walnut were expelled with the stool; sections of the growths stained well throughout; death from cachexia in 3 months. In the same way carcinomatous polyps were

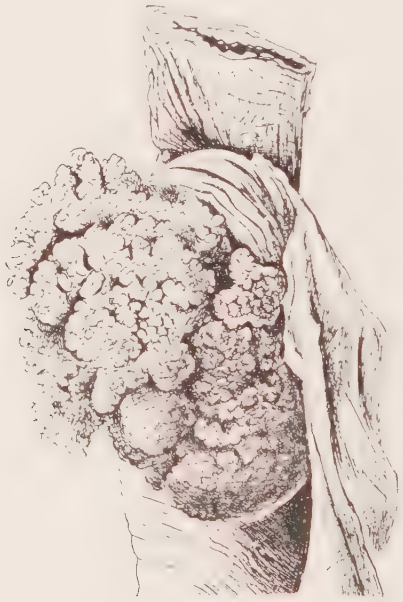
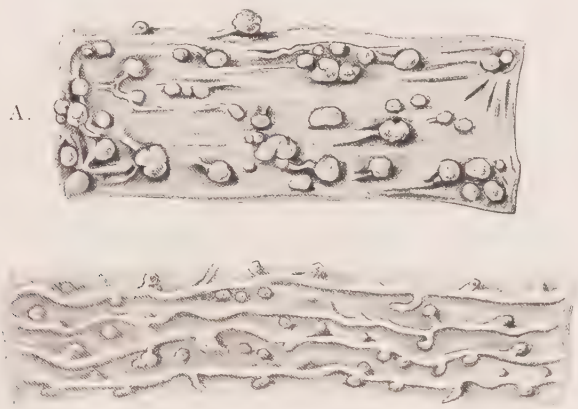


FIG. 378.—Large glandular polyp of sigmoid; invagination of the latter; virgin, 23 years old; ¾ nat. size.

passed by a 54 year old man, previous to which carcinomatous peritoneal metastasis had been demonstrated histologically; and by a 66 year old man who had suffered for some time with colicky difficulties (Adler, Drey). Cases of the second kind also may lead to invagination of the bowel, rectal prolapse and hemorrhages. Intestinal adenomatous polyposis involves the rectum in more than 80% of cases, occurs even in childhood and may be accompanied by profuse diarrhea, severe hemorrhages and colic. Heredity has been repeatedly observed, and the author saw numerous cases in one family. The evidence supports the idea of congenital predisposition on the basis of which these tumors develop at a later time. Another fact is that intestinal polyposis occurs in cases of tuberous sclerosis with multiple cardiac, renal and skin tumors.

In a 52 year old woman with polyposis of the stomach and intestines, and carcinoma of the rectum, the author saw multiple exostoses, a suprarenal struma and a cholesteatoma of the leptomenix of the pons (Hauser, Smoler, Jungling). Verse (lit.) assumes with Hauser, there is a congenital disposition on the part of the epithelial cell to a more marked proliferation which, by slight irritation (catarrh) leads to the formation of polyps (Oseki); according to Borelius and Sjovall, an inflammatory process precedes the polyposis; Ribbert, on the other hand, believes they develop as abnormalities (comp. Wechselmann, Peters). About one half of the cases (Quenu and Landel) have carcinomas, even children; according to our experience this combination is even more frequent, and according to Hauser, carcinomatous degeneration is the rule (cf. Wechselmann).




FIGS. 379 and 380.—Polyposis of bowel. A, piece of colon from woman 30 years old from whom a carcinoma of the rectum was operatively removed. The whole of small bowel and colon showed this polyposis; nat. size. B, Piece of ileum of man 62 years old with polyposis of stomach and the whole bowel; 7/8 nat. size.

For intestinal polyposis in dysentery or tuberculosis, see pp. 774 and 801.

Very minute pedunculated polyps, often in large numbers, are frequently seen, especially in status lymphaticus (pp. 499 and 260), but they are not adenomas, only raised, almost pedunculated follicles, without change in the glandular layers.

### Malignant Tumors

**Carcinoma.**— Primary carcinomas are the most important intestinal tumors. There are macro- and microscopic forms such as we have studied in the stomach (p. 694). The most frequent are cylindrical cell tumors (adenocarcinoma, and the much more rare carcinoma solidum cylindrocellulare), polypoid, or soft and proliferating which disintegrate and leave

bowl-shaped ulcers with bulging margins (fig. 382), or annular infiltrates with transitions to hard scirrhous forms (fig. 387). Other tumors are polymorphocellular, predominantly solid, round cell types, with soft medullary, or hard scirrhous forms. Both cylindrical cell and round cell carcinomas have each a mucoid form. True papillary or villous carcinomas are rare. Some scirrhous forms are quite small, annular, stenosing and produce shallow ulcers. The latter are relatively frequent in the lower part of the sigmoid of older people and are favorable operative risks (motility) with relatively good prognoses after removal. Scirrhous carci-

FIG. 381.—Polyposis of the intestine. Section from large intestine, the whole of which was filled with similar excrescences. On section they were composed of a fibrous stalk covered with large, tall, mucous-producing columnar cells. L. H. #1930.

nomas produce marked contraction and shortening of the parts. According to Schuchardt, the rectum (normally 13 to 15 cm.) may be shortened to 4 cm. (in syphilis and tuberculosis even to 3 cm.).

Medullary, round cell, quickly growing carcinomas are not always easily differentiated from sarcoma. The relatively rare mucoid carcinomas occur in all parts, but chiefly in the rectum, where also the common cylindrical cell carcinoma is numerically predominant (Kraske).

Rectal carcinoma is the most common intestinal carcinoma. The average age is 55 years; two-thirds occur in males. Pauchet calls it a benign cancer if recognized in time and removed by radical operation (mistaken for hemorrhoids and enteritis). The prognosis depends to a

considerable extent on the physician first consulted, *i.e.*, on whether careful rectal examination was made (Hirschmann, Krecke, Kuttner).

Mucoid carcinomas not rarely cause diffuse infiltrations up to the thickness of a fist, with total, jelly-like metamorphosis of the intestinal wall, finally, throughout the entire length of the rectum. They ulcerate early and on that account the lumen sometimes remains quite sufficient.

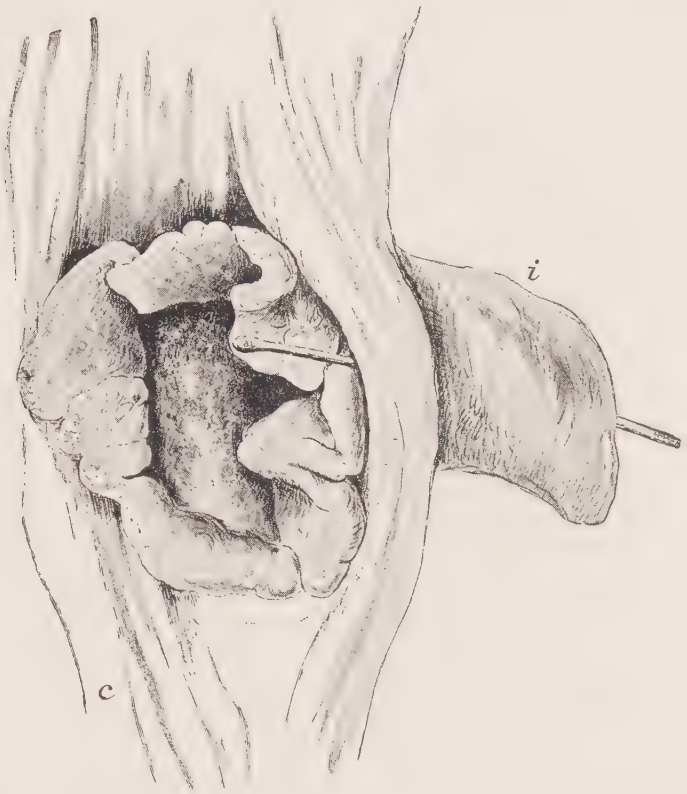



FIG. 382.—Bowl-shaped ulcerating cylindrical cell carcinoma (insular form) in cecum (c), near valve of Bauhin; probe in ileum (i); nat. size.

The rectum may resemble a thick-walled, rigid, and at the same time dilated tube (as though it had been curretted). Mucoid masses may appear in the feces. In other cases, a short annular, or a long stenosis, results (fig. 383). It is believed that mucoid carcinomas offer better chances for an operative radical cure than other carcinomas (Zimmer, lit.). Carcinomas of the rectum may also metastasize to the skin around the anus and occasionally involve the inguinal nodes. In a 22 year old man with a non-operated rectal carcinoma, the author saw the anus, scrotum, the root of the penis, and the skin as far as the inguinal region, nodular, ulcerated and infiltrated. Squamous cell carcinoma occurs in the lower

rectum from metaplastic epithelium of the rectum, from the epidermis at the end of the rectum (Bohm), or from congenitally sequestered islands of skin in the rectal mucosa (Foges, lit.). Pavement epithelial metaplasia also occurs, but rarely, in intestinal adenocarcinomas. Schmittmann described true cornified carcinoma of the ileo-cecal valve. The author has examined many polyps from the lowest part of the rectum, which were completely covered by pavement epithelium and the papillary connective tissue cores of which contained glands. Melano-carcinomas occur

FIG. 383.—Stenosing colloid carcinoma of rectum. The upper, markedly dilated bowel covered with numerous follicular ulcers is turned backward; man 33 years old (microscop. solid globocellular mucoid carcinoma). Nat. size.

in the ano-rectal region (Chalier & Bonnet, lit.). (Melano-sarcomas on p. 826.)

Adenomatous polyps may undergo carcinomatous change when the epithelial layer multiplies, becomes irregular, the nuclei become rich in chromatin and the cells penetrate into the submucosa (p. 809).

The favorite site of carcinoma is in the colon, especially at its narrow places and flexures, but it also occurs in the small bowel, especially in the duodenum near the papilla (lit. by Kanzler, Schlieps). In 2 cases in young women, the author found stenosing, almost circular carcinomas of

the ileum, roughly ulcerating in one case, which was a carcinoma cylindrocellulare solidum probably to be classed with basal cell carcinomas, *i.e.*, pronounced tendency to form large rounded angular cell nests with relatively straight or delicately bending small arcs peripherally bordered with cylindrical cells. Between the fibrous bundles of the muscular layers were long cell columns. In one case there were but minute traces of transition to adenocarcinoma; in the other pronounced formation of

FIG. 384.—Ulcerative carcinomat. stricture (c) of sigmoid (scirrhous cylindrical cell carcinoma) circular form. Enormous dilatation of colon above stricture (o); the lower narrow part U; A, appendices epiploica, carcin. infiltr.; fresh and older peritonitis starting from stricture; ⅓ nat. size.

cylindromas (hyalin filling) within the cell nests (carcinoma cylindrocellulare solidum cylindromatosum). For the first case, see fig. 307.

Arranged according to frequency: the rectum, above 60%,—colon (chiefly its flexures and cecum), duodenum, small bowel. Among 123 carcinomas of the intestines in the pathological institute of Basel, 51 were in the rectum, 36 in the colon, 28 the sigmoid flexure, 2 the ileum, 5 the duodenum (Fritz Muller). Among 1078 cases of carcinoma, 57, *i.e.*,

5.25% were in the rectum which occupies the 5th place in the scale of frequency, after the stomach, uterus, breast, esophagus. At the distal end of the appendix of a 31 year old servant girl who had died in the 4th week of typhoid fever, the author found a diffuse, solid, round cell carcinoma the size of a lead pencil which had completely invaded the muscularis. In a second case (32 year old woman who had suffered for some years at times with exacerbations of pain in the appendiceal region) the small

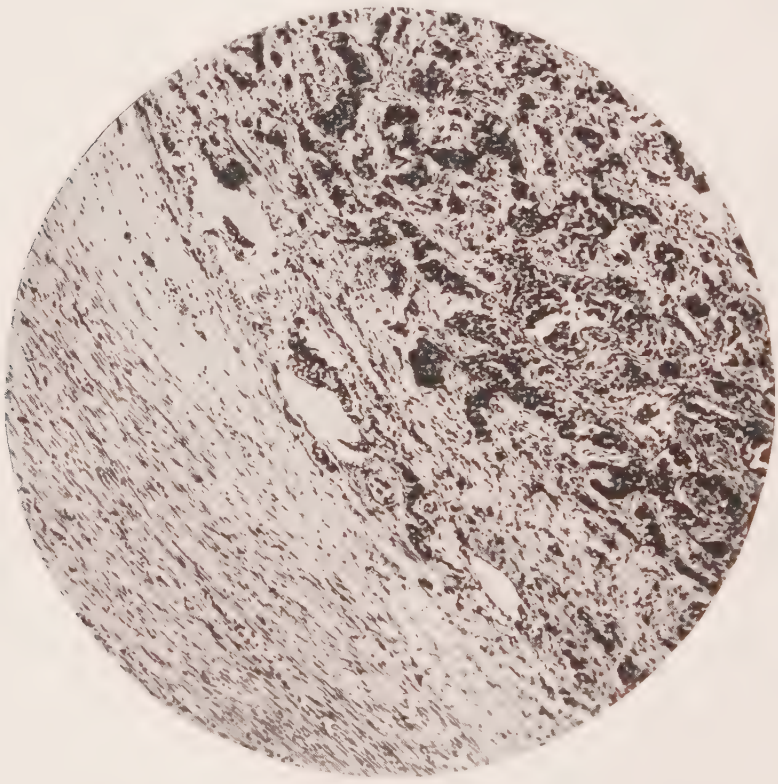


FIG. 385.—Primary small cell carcinoma of the vermiform appendix. In twenty thousand appendices examined in the Lankenau Hospital this tumor occurred in one-half of 1 %. It was never diagnosed clinically, was present in specimens showing all sorts of lesions, the majority were present near the tip and produced a bulbous shaped distal end. In many cases followed for five years and upwards no recurrences were noted. See text for discussion of the histogenesis. × 100. L. H. #6373.

thick appendix was infiltrated throughout all its layers by solid globo-cellular carcinoma; the muscularis was hypertrophic. Cylindrical cell solid carcinoma and round cell carcinoma seem to be more frequent in quite young individuals, and there are cases in which it is difficult to decide whether to speak of epithelioma or carcinoma of the small bowel; in older individuals there seem to be more adenocarcinomas and the mucoid forms, although the latter are relatively rare (see Miloslavich).

(*Continued in Second Volume.*)

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Heavy face type denotes an illustration.

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Heavy face type denotes an illustration.

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**Heavy face type denotes an illustration.**

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**Heavy face type denotes an illustration.**

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